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Department of Health and Human Services

Food and Drug Administration

21 CFR Part 130

Sulfiting Agents in Standardized Foods; Labeling Requirements; Proposed Rule

21 CFR Parts 182 and 184

Sulfiting Agents; Affirmation of GRAS Status; Proposed Rule

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 130

[Docket No. 84N-0103]

Sulfiting Agents in Standardized Foods; Labeling Requirements

AGENCY: Food and Drug Administration.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing a regulation that will require that when sulfiting agents have a functional effect in a standardized food or when they are present in a standardized food at a detectable level, their presence must be declared on the label of that food. The proposed regulation states that a detectable level of sulfites is 10 parts per million (ppm) or more. It also sets forth the circumstances under which FDA proposes to find that a standardized food that contains indirectly added sulfiting agents conforms to the applicable standard even though no provision for sulfites is made in that standard. Published elsewhere in this issue of the **Federal Register** is a proposed rule affirming, with specific limitations, that certain uses of sulfiting agents are generally recognized as safe. With FDA's previous rulemakings concerning sulfiting agents and the two proposed rules published in this issue of the **Federal Register**, the agency believes that it has addressed the most significant sources of concern about the use of sulfites in food in ways that will minimize the potential for allergic-type responses.

DATE: Comments by February 17, 1989.

ADDRESS: Written comments to the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Elizabeth J. Campbell, Center for Food Safety and Applied Nutrition (HFF-312), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202-485-0229.

SUPPLEMENTARY INFORMATION:

I. Background

A. Labeling of Sulfites in Nonstandardized Foods

Recent scientific developments have shown that sulfiting agents (sulfur dioxide, sodium sulfite, sodium and potassium bisulfite, and sodium and potassium metabisulfite) in food can cause allergic-type responses in a significant minority of the population. Responses have been reported that have ranged from mild discomfort to life-threatening episodes. It is essential, therefore, that sulfite-sensitive individuals be protected from unexpected exposure to these ingredients.

Section 403(i)(2) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 343(i)(2) requires that all of the ingredients in a nonstandardized food be declared on the label of that food by their common or usual names unless FDA has exempted the ingredients from that requirements. FDA has established such an exemption in 21 CFR 101.100(a)(3) for "incidental additives" that are present in foods at insignificant levels and that do not have any technical or functional effect in the foods. In the absence of specific guidance from FDA, sulfites generally have been treated by manufacturers as incidental additives whose presence did not have to be declared on labels except when they were directly added to a food for a technical effect.

As a result of evidence that sulfites can cause allergic-type responses, however, FDA decided that consumers should be advised when these ingredients are present in foods. In the **Federal Register** of July 9, 1986 (51 FR 25012), the agency adopted 21 CFR 101.100(a)(4), which states that sulfiting agents will be considered to be present in foods in insignificant amounts only if no detectable amount of sulfite is present in the finished food. Section 101.100(a)(4) states that a detectable amount of a sulfiting agent is 10 ppm or more. This regulation became effective on January 9, 1987. It requires that the presence of detectable amounts of sulfiting agents be declared on the labels of all foods that are subject to the requirements of 21 U.S.C. 343(i). When a sulfiting agent is added directly to a nonstandardized food, it must be declared on the label by its common or usual name. In the preamble to the final rule, however, FDA stated that where sulfiting agents are added indirectly to the food and do not have a technical or functional effect on the food, the collective term "sulfiting agents" may be declared on the label rather than the common or usual name of the specific sulfiting agents. (See paragraph 14 under "Other Comments" (51 FR 25012 at 25015).) The regulation left open the question of the treatment of sulfites on the labels of many standardized foods.

B. Labeling Sulfites in Standardized Foods

A food that is represented to be or purports to be a standardized food is misbranded under section 403(g) of the act (21 U.S.C. 343(g)) unless (1) it conforms to the relevant definition and standard, and (2) its label bears the common or usual names of optional ingredients (other than spices, flavoring, and coloring) required to be listed by the standard.

1. Standardized Foods Subject to Optional Ingredient Listing Requirement

In recent years, FDA has amended many of its regulations for standardized foods to make all ingredients optional. This change has meant that the common or usual names of each of the ingredients must be declared on the label in accordance with the provisions of 21 CFR Part 101. As a result, components of these ingredients, such as sulfiting agents, must be declared on the labels of foods unless the components qualify for the incidental additive ingredient labeling exemption of § 101.100(a)(3) (21 CFR 101.100(a)(3)). Under § 101.100(a)(4)) (21 CFR 101.100(a)(4)), however, detectable amounts of sulfiting agents cannot qualify for this exemption.

2. Standardized Foods Not Subject to Ingredient Listing Requirements

FDA has not amended all of its regulations for standardized foods in this manner. The unamended regulations have no provisions addressing the need for label declaration of sulfiting agents. Some standards allow sulfiting agents to be present but do not require the listing of these ingredients on the label. For example, the standards for glucose sirup (21 CFR 168.120) and dried glucose sirup (21 CFR 168.121) permit the presence of 40 milligrams per kilogram (40 parts per million) or less of sulfur dioxide, but these standards have no sulfur dioxide listing requirement. Other standards do not directly provide for the presence of sulfiting agents, but sulfiting agents may be present in the food as components of permitted ingredients.

This situation is of concern to FDA because if the presence of the sulfiting agents is not declared on the label of a food, a sulfite-sensitive individual could be misled into believing that he or she can eat that food without risk.

3. Standardized Foods in Which Sulfiting Agents Are Components of Ingredients

Under 21 CFR 130.8(a), a food does not conform to a definition and standard of identity if it contains an ingredient for which no provision is made in such standard, "unless such ingredient is an incidental additive introduced at a nonfunctional and insignificant level as

a result of its deliberate and purposeful addition to another ingredient permitted by the terms of the applicable standard and the presence of such incidental additive in unstandardized foods has been exempted from label declaration as provided in § 101.100 of this chapter."

Sulfiting agents are frequently used in foods that are intended to become ingredients of standardized foods. Before the adoption of 21 CFR 101.100(a)(4), many firms that produced standardized foods with sulfite-treated ingredients assumed that if the sulfiting agents had no effect in the finished food, and if the sulfites were used in the ingredient in accordance with current good manufacturing practice, the sulfiting agents were incidental additives. These firms also concluded that under 21 CFR 130.8(a), the finished foods complied with the relevant food standards, despite the fact that there was no provision for the sulfiting agents in the standard.

In adopting 21 CFR 101.100(a)(4), FDA took the position that sulfiting agents in amounts of 10 ppm or more were significant. As a result, there are a number of foods that technically do not conform to the relevant standards of identity because these foods contain sulfiting agents that are not provided for in the standards and that are not incidental additives.

FDA recognizes that it could declare such foods to be misbranded until they are reformulated, or until the standards are amended to provide for the presence of sulfites. However, the agency has concluded that such action would make little sense. It would mean a significant disruption in the food supply for a violation that would not have any health significance if the presence of the sulfiting agents were declared on the label of the food.

II. Requirement To Declare Presence of Sulfites in Standardized Foods

A. The Proposed Action

To ensure that consumers can determine at point of sale whether any food, standardized or nonstandardized, contains added sulfites, FDA is proposing to amend its regulations to require that the presence of sulfiting agents be declared on the label of all standardized foods that contain an amount of these ingredients that has a functional effect in the food or that is detectable. (If the sulfiting agents have a technical effect in the food, their use must, of course, be consistent with the standard of identity, or the food would be adulterated under 21 U.S.C. 343(g)(1)).

Proposed § 130.9(a) states that any standardized food that contains a sulfiting agent that has a functional effect or that is present at a level of 10 ppm or more in the finished food [1] is misbranded unless the presence of the sulfiting agent is declared on the label. This provision will require that the presence of the sulfiting agent be declared even if the relevant standard does not require the listing of optional ingredients, and even if the sulfiting agent has been indirectly incorporated into the food as, for example, a component of an optional or required ingredient or as a processing aid. Failure to declare the presence of the sulfiting agent will render the food misbranded.

B. Legal Basis

FDA believes that this proposal is fully consistent with the act. Under section 403(a) of the act (21 U.S.C. 343(a)), a food is misbranded if its labeling is false or misleading in any respect. Under section 201(n) (21 U.S.C. 321(n)), the extent to which labeling fails to reveal facts material with respect to the consequences of use of an article shall be taken into account in determining whether the labeling of that article is misleading. Because, as stated above, sulfiting agents can cause allergic-type responses of unpredictable severity, the presence of a detectable amount of sulfites (as defined by 21 CFR 101.100(a)(4) as 10 ppm or more sulfites) in a food is a material fact. Therefore, the absence on the label of a food of the material fact that the food contains sulfiting agents renders that label misleading and the food misbranded under sections 403(a) and 201(n) of the act.

C. Means of Compliance

FDA recognizes that the labels of many standardized foods do not bear an ingredient list. Only those foods whose standard of identity requires the listing of optional ingredients will bear such a list.

Should the agency adopt this proposal, it will consider the regulation to be satisfied if the presence of the sulfiting agent is declared prominently on the label. Four situations seem likely:

If there is no ingredient list on the label, and the sulfites are directly added to the food, a statement such as "This food contains (common or usual name of sulfiting agent)" should be placed on the label.

If the sulfiting agent is directly incorporated in the food as a preservative, under section 403(k) of the act (21 U.S.C. 343(k)), the declaration of the presence of the sulfiting agent must be accompanied by an appropriate statement of this fact (e.g., "With (common or usual name of sulfiting agent), a preservative;" "Contains _____, a preservative;" or "to retard spoilage").

If the sulfiting agent is indirectly incorporated in a standardized food whose standard requires the listing of all ingredients in accordance with Part 101, the presence of the sulfiting agents is declared on the label in accordance with 21 CFR 101.4 (a) and (b)(2). However, FDA will not take action against these foods if the sulfites are listed in parentheses following the name of the food of which they are a component, for example, "_____ (with added (common or usual name of sulfiting agent))."

If the sulfiting agents are indirectly incorporated in a standardized food whose standard does not require the listing of all ingredients, the presence of the sulfiting agents is declared prominently on the label. A statement such as "An ingredient in this food contains added (common or usual name of sulfiting agent)" or "Contains _____ with added (common or usual name of sulfiting agent)" may be utilized.

In the preamble to the final rule that published in the **Federal Register** of July 9, 1986 (51 FR 25012), requiring that the presence of detectable amounts of sulfiting agents be declared on the labeling of nonstandardized foods, the agency discussed flexibility concerning the declaration of sulfiting agents. (See paragraph 14 under "Other Comments" (51 FR 25012 at 25015.) FDA announced that, with respect to sulfiting agents that are directly added to, or that have a technical effect in, food, the name of the specific sulfiting agent that is added must be declared on the label. However, the agency agreed that some flexibility is warranted in the declaration of sulfiting agents that are indirectly added to a food and that have no technical or functional effect in the food. An

[1] The term "finished food" refers to the food as it is packaged and sold. The term also refers to food sold to be further processed, mixed, or repackaged, unless there is a written agreement between the shipper and the receiver of the food (in accordance with the provisions of 21 CFR 101.100(d)) that contains the information necessary for appropriate labeling of the food. However, the term "finished food" does not refer to the food as it will ultimately be consumed. Thus, dehydrated finished foods must declare the presence of sulfiting agents without consideration of further rehydration treatment before consumption. Also, the term "finished food" does not refer to portions of the food that are inedible or invariably discarded (e.g., shells from shellfish and crustaceans and packing mediums for products such as cooked lobster meat in brine). Such portions will be excluded from sulfite analyses. Where packing mediums may be used for other home recipes (e.g., canned clam medium in dips) however, the packing medium will not be excluded from sulfite analysis.

indirectly added sulfite is present in a food as a component of an ingredient in the food, as a processing aid, or as a migrant from food packaging. The purpose of declaring sulfiting agents that are indirectly added and that have no technical or functional effect is to provide information to the consumer who wishes to avoid foods that contain sulfites. The agency stated that it will consider amending the regulations in which collective terms permitted in ingredient declarations are listed (21 CFR 101.4(b)) to include a collective term for the sulfiting agents. However, pending promulgation of a provision in § 101.4(b), the agency will not take legal action against standardized foods that declare sulfiting agents as follows: (1) when sulfiting agents remain in a food in a significant amount but no longer have a technical or functional effect, they may be declared by the term "sulfiting agents;" and (2) when a food contains a sulfiting agent that has a technical or functional effect in the food and that is declared in the list of ingredients by its common or usual name, any nonfunctional sulfiting agents present in the food need not be declared separately in the list of ingredients. However, FDA emphasizes that this flexibility applies only if the sulfite is indirectly added and does not perform a technical or functional effect in the food.

The agency also advises that there is no requirement for quantitative declaration of sulfites. The only information that is required to be included in the label is the name of the sulfiting agent, or, in the circumstances explained in the preceding paragraph, the term "sulfiting agents."

The agency specifically solicits comments as to whether consumers are aware of the common or usual names of the specific sulfiting agents, particularly sulfur dioxide, and whether consumers understand that if they are sulfite-sensitive, they should avoid foods containing any of these sulfiting agents. FDA also solicits comments as to whether the agency should include in any final rule a requirement that where the specific sulfiting agent is declared on the label by its common or usual name, this common or usual name must be followed by the term "a sulfiting agent." For example: "contains sulfur dioxide (a sulfiting agent)."

III. Compliance With Standard of Identity

FDA is also acting to remove the uncertainty about the status of standardized foods to which sulfites are indirectly added at levels that have no technical effect. The agency is proposing in § 130.9(b) to find that standardized foods that contain sulfites that would have been considered to be incidental additives before the adoption of § 101.100(a)(4) are not misbranded under 21 U.S.C. 343(g)(2) so long as:

(1) The sulfiting agents in the finished standardized food are nonfunctional;

(2) The sulfiting agents have indirectly become components of the standardized food as a result of a use that is in accordance with current good manufacturing practice; and

(3) The presence of the sulfiting agents in the standardized food is declared on the label. Such declaration should be made in accordance with the principles outlined above.

FDA considers this proposed finding to be fully consistent with the act. Under section 306 of the act (21 U.S.C. 336), FDA has discretion not to take action against minor violations of the act if it finds that the public interest will be adequately served by a suitable notice or warning. The failure of a food to comply with the applicable standard of identity because it contains nonfunctional levels of sulfiting agents is a minor violation so long as the public, particularly sulfite-sensitive individuals, are made aware of the presence of sulfiting agents in the food by an appropriate label statement. Such a statement provides adequate notice to sulfite-sensitive individuals of the risks that they face if they consume the food product.

IV. Effective Date

Consistent with its action in adopting the final rule requiring that the presence of detectable amounts of sulfiting agents be declared on the labels of nonstandardized foods (21 CFR 101.100(a)(4)), FDA proposes that this regulation to establish similar requirements for standardized foods become effective 6 months after publication of the final rule rather than on the next uniform effective date for compliance with new food labeling requirements that is periodically announced. Thus, the agency proposes that by 6 months after the date of publication of any final regulation, all finished foods in which a sulfiting agent has a technical or functional effect, or in which there is a detectable amount of a sulfiting agent, that are initially introduced or initially delivered for introduction into interstate commerce must bear labeling that declares the presence of the sulfiting agent. The agency recognizes that this proposed regulation would require some manufacturers who do not declare sulfites on the labels of their products to revise their labels. Nonetheless, FDA is proposing the 6-month effective date because information about the presence of sulfiting agents is not merely informative but is necessary to protect the health of sensitive individuals. On the basis of its experience, the agency believes that 6 months is an adequate amount of time for manufacturers to change their labeling. The agency urges manufacturers and distributors of standardized foods, however, to declare sulfiting agents on their labels as soon as possible.

Consistent with the agency's response to a similar 6-month effective date for the labeling requirements for nonstandardized foods (see paragraph 16 under "Other Comments" (51 FR 25012 at 25016)), this proposed labeling regulation has as its basis a serious health concern. Although FDA is sympathetic to the problems processors may encounter with a 6-month effective date, the agency cannot ignore the potential hazard to sulfite-sensitive consumers. The labeling requirement in this proposed regulation will apply to foods that are initially introduced into interstate commerce after the effective date of any final rule. If it adopts this regulation, the agency will not take action against foods that are in interstate commerce on the effective date of the final rule.

The agency, however, specifically solicits comments on the appropriateness of the proposed 6-month effective date.

V. Economic Impact

In accordance with section 605(b) of the Regulatory Flexibility Act, the agency has considered the effect that this proposed rule would have on small entities including large and small businesses and has determined that the proposed labeling requirements will not result in a significant impact on a substantial number of small entities. Furthermore, in accordance with Executive Order 12291, the agency has analyzed the economic effects of this regulation and has determined that the rule, if promulgated, will not be a major rule as defined by that Order.

A copy of the threshold assessment supporting this determination is on file with the Dockets Management Branch (address above).

VI. Environmental Impact

The agency has determined under 21 CFR 25.24(a)(11) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

VII. Paperwork Reduction Act of 1980

Section 130.9 of this proposed rule contains collection of information requirements. As required by section 3504(h) of the Paperwork Reduction Act of 1980, FDA has submitted a copy of this proposed rule to the Office of Management and Budget (OMB) for its review of these collection of information requirements. Other organizations and individuals desiring to submit comments on the collection of information requirements should direct them to FDA's Dockets Management Branch (address above) and to the Office of Information and Regulatory Affairs, OMB, Rm. 3208, New Executive Office Bldg., Washington, DC 20503, Attn: Desk Officer for FDA.

VIII. Submission of Comments

Interested persons may, on or before February 17, 1989, submit to the Dockets Management Branch (address above) written comments regarding this proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

In addition to requesting comments concerning the proposal in its entirety, the agency solicits specific comments concerning consumer awareness of the common or usual names of sulfiting agents, particularly sulfur dioxide; consumer understanding of the need of sulfite-sensitive individuals to avoid foods containing any of these sulfiting agents; whether FDA should include in any final rule a requirement that where the specific sulfiting agent is declared on the label be its common or usual name, this common or usual name must be followed by the term "a sulfiting agent;" and the appropriateness of the proposed 6-month effective date.

List of Subjects in 21 CFR Part 130

Food additives, Food grades and standards.

Therefore, under the Federal Food, Drug, and Cosmetic Act, it is proposed that Part 130 be amended as follows:

PART 130—FOOD STANDARDS: GENERAL

1. The authority citation for 21 CFR Part 130 is revised to read as follows:

Authority: Secs. 201(n) and (s), 306, 401, 403, 701, 52 Stat. 1041 as amended, 72 Stat. 1784 as amended, 52 Stat. 1045–1046, 1047–1048 as amended, 1055–1056 as amended (21 U.S.C. 321(n) and (s), 336, 341, 343, 371); 21 CFR 5.11.

2. New § 130.9 is added to Subpart A to read as follows:

§ 130.9 Sulfites in standardized food.

(a) Any standardized food that contains a sulfiting agent or combination of sulfiting agents that is functional and provided for in the applicable standard or that is present in the finished food at a detectable level is misbranded unless the presence of the sulfiting agent or agents is declared on the label of the food. A detectable amount of sulfiting agent is 10 parts per million or more of the sulfite in the finished food. The level of sulfite in the finished food will be determined using sections 20.123 through 20.125, "Total Sulfurous Acid," in "Official Methods of Analysis of the Association of Official Analytical Chemists," 14th ED. (1984), which is incorporated by reference in accordance with 5 U.S.C. 552(a), and the refinements of the "Total Sulfurous Acid" procedure in the "Monier-Williams Procedure (with Modifications) for Sulfites in Foods," which is Appendix A to Part 101 of this chapter. A copy of sections 20.123 through 20.125 of the "Official Methods of Analysis of the Association of Official Analytical Chemists" is available from the Association of Analytical Chemists, 1111 North 19th St., Suite 210, Arlington, VA 22209, or available for inspection at the Office of the Federal Register, 1100 L St. NW., Washington, DC.

(b) Any standardized food that, as a result of actions that are consistent with current good manufacturing practice, contains an indirectly added sulfiting agent that has no functional effect in the food and that would, in the absence of § 101.100(a)(4) of this chapter, be considered to be an incidental additive for purposes of § 130.8, conforms to the applicable definition and standard of identity if the presence of the sulfiting agent is declared on the label of the food.

Frank E. Young,

Commissioner of Food and Drugs.

Otis R. Bowen,

Secretary for Health and Human Services.

Dated: August 22, 1988.

[FR Doc. 88–29032 Filed 12–16–88; 8:45 am]

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21 CFR Parts 182 and 184

[Docket No. 81N–0314]

Sulfiting Agents; Affirmation of GRAS Status

AGENCY: Food and Drug Administration.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is proposing to affirm, with specific limitations, that certain uses of sulfur dioxide, sodium sulfite, sodium and potassium bisulfite, and sodium and potassium metabisulfite (collectively known as "sulfiting agents" or "sulfites") are generally recognized as safe (GRAS). This action is based upon FDA's review of all available information on sulfiting agents including new information on sulfiting agents received in response to a proposal to affirm the GRAS status of sulfiting agents published in the **Federal Register** of July 9, 1982 (47 FR 29956); the January 31, 1985, final report of the Federation of American Societies for Experimental Biology (FASEB) on the Reexamination of the GRAS Status of Sulfiting Agents; the hearing conducted by the Advisory Committee on Hypersensitivity to Food Constituents; recently published reports in the medical literature; and other relevant information.

DATE: Comments by February 17, 1989.

ADDRESS: Written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Robert L. Martin, Center for Food Safety and Applied Nutrition (HFF–334), Food and Drug Administration, 200 C St. SW., Washington, DC 20204, 202–426–9463.

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I. Background/Regulatory History

A. Select Committee Review and 1982 Proposal

In the **Federal Register** of July 9, 1982 (47 FR 29956) (Ref. 1), FDA proposed to affirm, with specific limitations, the GRAS status of the use of sulfur dioxide, sodium bisulfite, and sodium and potassium metabisulfite. The document also proposed to delete sodium sulfite and potassium bisulfite from the list of substances whose use is GRAS because the agency believed that use of these substances had been discontinued except for the known food additive use, under 21 CFR 173.310, of sodium sulfite as a boiler water additive.

The agency based its 1982 proposal on a report on the health aspects of the use of sulfiting agents as food ingredients (Ref. 2) issued by the Select Committee on GRAS Substances (the Select Committee) of FASEB in 1976, during the agency's review of the safety of GRAS substances (Ref. 3). That report presented an analysis of human exposure and toxicological date on sulfiting agents and was based partly on a review of available scientific literature from 1920 through 1972 (Ref. 4). The report stated that it was reasonable to conclude that the daily intake of sulfur dioxide from sulfited foods consumed in the United States did not exceed 2 milligrams per kilogram of body weight for adults and probably was not more than 0.2 milligram per kilogram for the great majority of the population.

The 1976 report surveyed all the available toxicological data on sulfites, including data on metabolism, acute and chronic oral toxicity, other long-term studies, teratology, carcinogenicity, and mutagenicity. On the basis of this review, the Select Committee concluded that:

> There is no evidencde in the available information on potassium bisulfite, potassium metabisulfite, sodium bisulfite, sodium metabisulfite, sodium sulfite and sulfur dioxide that demonstrates, or suggests reasonable grounds to suspect, a hazard to the public when they are used at levels that are now current and in the manner now practiced. However, it is not possible to determine, without additional data, whether a significant increase in consumption would constitute a dietary hazard.

In the 1982 proposal, the agency stated that it had undertaken its own evaluation of all available information on sulfiting agents. It supplemented the Select Committee's exposure data on sulfites with more recent data obtained by the National Academy of Science/National Research Council (NAS/NRC) in 1977 (Ref. 5).

The agency tentatively concluded in the 1982 proposal that, based upon the available safety data, potassium metabisulfite, sodium bisulfite, sodium metabisulfite, and sulfur dioxide should be affirmed as GRAS with specific limitations. The agency proposed not to affirm potassium bisulfite and sodium sulfite as GRAS because it did not possess any evidence of food use for potassium bisulfite nor sufficient information relating to the uses of sodium sulfite as a GRAS food ingredient. Therefore, the agency could not establish limitations on the use of these two sulfiting agents.

The comment period for the 1982 proposal closed on September 7, 1982. In the **Federal Register** of November 2, 1982 (47 FR 49666), FDA extended the comment period to December 7, 1982, in response to two requests for extensions. Since the extended comment period closed, the agency has continued to receive comments regarding sulfiting agents.

The agency has received a large number of comments from consumers, Congressional representatives on behalf of consumers, health professionals, consumer groups, and State government officials that reported the possibility that some susceptible individuals may experience allergic-type responses after consuming food treated with sulfiting agents. (The agency is using the term "allergic-type responses" to describe the range of symptoms that individuals have suffered after eating certain sulfite-treated foods. These symptoms resemble the symptoms of a response to an allergen. The scientific community, however, is unsure at this time about the actual mechanism by which a response is elicited by the sulfite ingredient.) These responses have ranged from mild discomfort to life-threatening episodes.

On October 28, 1982, the agency received a citizen petition regarding the use of sulfiting agents in food and drugs. This petition addressed the problems of exposure of sensitive individuals to sulfites in foods and drugs. It expressed concern about the possibility that unsuspecting sulfite-sensitive individuals might have a severe response after eating foods or taking medications that contain sulfiting agents. The petition urged the agency to take certain regulatory steps to restrict the use of sulfites in food and drugs.

B. Health Concerns and FASEB Review

The new information that the agency received in response to its 1982 proposal raised public health concerns for two reasons. First, this information raised the possibility of severe and unpredictable allergic-type responses in a significant subgroup of the U.S. population. Second, it revealed that the number of uses and the levels of use of sulfiting agents had significantly increased in the U.S. food supply since the survey relied upon by the Select Committee was taken. This new information prompted the agency to ask FASEB to reexamine the GRAS status of the use of sulfiting agents.

FASEB established an ad hoc Review Panel on the Reexamination of GRAS Status of Sulfiting Agents (the Panel). On July 9, 1984 (49 FR 27994), FDA announced the formation of the Panel. The agency asked FASEB to have the Panel address the following question:

> In view of the currently available information relevant to the use and safety of sulfiting agents, which of the five types of conclusions for the appraisal of GRAS substances that were developed by the Select Committee now applies to the use of sulfiting agents? The conclusion which is reached should be supported by the discussions of the rationale behind the conclusion.

The Panel evaluated recent scientific publications and new information and data submitted to FDA in response to its 1982 proposal. The Panel supplemented this information with additional

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materials that it acquired independently. The Panel conducted an open meeting on November 29, 1984, at which individuals and organizations presented their views on sulfite-related issues. On January 31, 1985, the Panel issued its final report (Ref. 6).

In that report, the Panel concluded that for the majority of the population, "there is no evidence in the available information * * * that demonstrates or suggests reasonable grounds to suspect a hazard." The Panel further concluded, however, that for the fraction of the public that is sulfite sensitive, "there is evidence in the available information * * * that demonstrates or suggests reasonable grounds to suspect a hazard of unpredictable severity to such individuals when they are exposed to sulfiting agents in some foods at levels that are now current and in the manner now practiced." (Ref. 6, p. 60.)

An analysis of consumer complaints compiled by FDA and made available to the Panel indicated that the majority of incidents involving allergic-type responses to sulfites in food could be attributed to sulfited fruits and vegetables that are intended to be served raw or sold raw to consumers or are presented to consumers as fresh and to certain sulfited potatoes and potato products. Thus, the Panel determined that, although most uses of sulfites on food appear to present no safety concerns for most people, certain uses of these ingredients, particularly on popular unlabled food items often consumed in food-service establishments, could present a significant risk for some sulfite-sensitive individuals.

C. FDA's Response

Based on the Panel's findings and on its own review of the available evidence, FDA took several actions to minimize the risk to health from the use of sulfiting agents. The agency's first action was to move to provide indivduals who know that they are sulfite-sensitive with the information that they need to avoid certain processed foods that contain sulfites. In the **Federal Register** of April 3, 1985 (50 FR 13306), FDA proposed to clarify the circumstances in which sulfiting agents could be considered to be incidental additives under 21 CFR 101.100(a)(3) (Ref. 7). That rulemaking was published as a final rule in the **Federal Register** of July 9, 1986 (51 FR 25012) (Ref. 8).

Under § 101.100(a)(3), substances that are present in a food at insignificant levels and that do not have any functional effect in that food are incidental additives and thus are exempt from being declared in the list of ingredients. In the July 9, 1986, final rule, FDA added § 101.100(a)(4), which provides that added sulfiting agents are present in food in an insignificant amount only if no detectable amount of these substances is present in the finished food. The regulation defines a detectable amount of a sulfiting agent as 10 parts per million (ppm) or more of the sulfite in the finished food when analyzed under the modified Monier-Williams procedure, which is set forth in Appendix A to Part 101. As a result of this rulemaking, sulfiting agents must be listed on the labels of nonstandardized foods when they are present at detectable but nonfunctional levels in the foods.

Sulfiting agents present at functional levels in nonstandardized foods have always been required to be declared in ingredient lists because these ingredients have never been exempted from Part 101 labeling requirements. In addition, sulfiting agents present as optional ingredients in standardized foods whose standards require the listing of optional ingredients in accordance with Part 101 have also always been required to be declared.

Elsewhere in this issue of the **Federal Register**, FDA is publishing a proposal to clarify the circumstances in which the presence of sulfiting agents in other standardized foods must be declared on the label. That notice proposes that sulfiting agents be listed on the label of these foods whenever they have a functional effect in these foods, or when they remain in the finished food at detectable levels. The agency believes, after a preliminary review, that the presence of the sulfiting agents should be declared in these circumstances because sections 201(n) and 403(a) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 321(n) and 343(a)) provide that labeling is misleading if it fails to reveal facts material with respect to the consequences of use of the article. The presence of sulfiting agents may create a hazard of unpredictable severity for individuals sensitive to these ingredients and is consequently a material fact. Thus, the agency's preliminary view is that the failure to declare the presence of a detectable amount of a sulfiting agent would render the label misleading.

The proposal also addresses the circumstances in which foods that fail to conform to the relevant standards of identity because they contain sulfiting agents that had been considered to be incidental additives under 21 CFR 130.6 before the adoption of 21 CFR 101.100(a)(4) will be considered to be misbranded under 21 U.S.C. 343(g). The agency's preliminary view is to not consider such foods to be misbranded if the presence of the sulfiting agents is declared on the label.

In addition to clarifying how foods that contain sulfiting agents must be labeled, the agency published a proposal in the **Federal Register** of August 14, 1985 (50 FR 32830), that announced its preliminary conclusion that the use of sulfiting agents on fruits and vegetables intended to be served raw or sold raw to consumers cannot be considered GRAS (Ref. 9a). Subsequently the agency published in the **Federal Register** of July 9, 1986 (51 FR 25021), a final rule confirming its preliminary conclusion and amending the regulations to except the use of sulfiting agents on fruits and vegetables intended to be served raw or sold raw to consumers from the uses of these substances that are GRAS (Ref. 9b). FDA took this action to address the sources of sulfite exposure that the agency found were associated with the greatest number of allergic-type responses.

In addition, the agency proposed in the **Federal Register** of December 10, 1987 (52 FR 46988), to revoke the GRAS status of the use of sulfites on "fresh" potatoes served or sold unpackaged and unlabeled to consumers (Ref. 10). In that proposal, the agency also asked for information about the other uses of sulfites on potatoes. That proposal is intended to control another major source of sulfite exposure that has been associated with severe allergic-type responses in sulfite-sensitive persons.

With those rulemakings, the agency believes that it has addressed the most significant sources of concern about the use of sulfites on food and, thus, has adequately responded to the concerns raised by the Panel. The primary purpose of the present rulemaking, therefore, is to announce the agency's tentative determination that the remaining uses of sulfiting agents, except those uses on meats and on foods that are significant sources of thiamine, are GRAS.

II. Uses of Sulfiting Agents on Food Products

A. Technical Effects

Sulfiting agents have numerous uses in food. They have been used for centuries in food processing as sanitizing (disinfection) agents for food containers and fermentation equipment. They have been used as preservatives to reduce or to prevent microbial spoilage of food; as selective inhibitors of undesirable microorganisms by the fermentation industries; and as antioxidants and inhibitors of enzyme-

catalyzed oxidative discoloration and nonenzymatic browning during the preparation, storage, and distribution of many foods. They also are used as dough conditioners, bleaching agents, processing aids, and pH control and stabilizing agents (Ref. 11). To accomplish these purposes, sulfiting agents are added directly to certain fresh foods or are added under controlled conditions during processing of some foods.

B. Currently Regulated Uses and Use Levels of Sulfites

Existing regulations state that the use of potasium bisulfite (21 CFR 182.3616), potasium metabisulfite (21 CFR 182.3637), sodium bisulfite (21 CFR 182.3739), sodium metabisulfite (21 CFR 182.3766), sodium sulfite (21 CFR 182.3798), and sulfur dioxide (21 CFR 182.3862) is GRAS, except when they are used in meats or foods recognized as a source of thiamine (vitamin B_1), or on fruits or vegetables intended to be served raw or sold raw to consumers or to be presented to consumers as fresh. Other sections that refer to the use of sulfiting agents are as follows: caramel (21 CFR 73.85(a)(2)(iii)); dextrose monohydrate (21 CFR 168.111(b)(2)); glucose sirup (21 CFR 168.120(b)(2)); food starch-modified (21 CFR 172.892(b)); boiler water additives (21 CFR 173.310(c)); cellophane (21 CFR 177.1200(c)); and water-insoluble hydroxyethyl cellulose film (21 CFR 177.1400). The Bureau of Alcohol, Tobacco and Firearms (BATF) lists sulfites as materials authorized for treatment of wine (27 CFR 240.1051).

The listings for dextrose monohydrate, glucose sirup, and food starch-modified limit residual sulfur dioxide concentrations in these products to not more than 20, 40, and 500 ppm, respectively. The Food Chemicals Codex (3d Ed.) specifications place an upper limit of 80 ppm residual sulfure dioxide in modified food starches (Ref. 12).

The agency did not set specific limits for levels of use of sulfiting agents in the current GRAS regulations (21 CFR Part 182). Rather, the regulations on these ingredients in Part 182 invoke the concept of "good manufacturing practice" (defined in § 182.1), which restricts the quantity of a substance that can be added to food to a level that does not exceed that reasonably required to accomplish the intended technical effect.

It is important to note that the level of sulfiting agent added to a particular food (the "treatment level") may differ considerably from the level of sulfiting agent remaining on that food at the time processing is complete (the "residual level"). The residual levels of sulfites in finished foods are generally lower than the amount of sulfites added during processing because during processing, sulfites can combine with other food components, may be liberated as sulfur dioxide, or may be oxidized to sulfate. Although good manufacturing practice based on treatment levels may be more convenient for food processors, limits on residual levels of sulfites in finished foods are better suited for public health protection. For that reason, the agency is basing the regulations of this rulemaking on residual levels of sulfites measured as sulfur dioxide equivalents found in the finished food product. (A sulfur dioxide equivalent is defined as that proportion of the weight of a sulfiting agent that can dissociate into sulfur dioxide. It provides a uniform and scientifically consistent means by which the sulfite content of foods can be reported.)

C. Prior Sanctions for the Use of Sulfites on Foods

Section 201(s)(4) of the act (21 U.S.C. 321(s)(4)) exempts from the definition of a food additive "any substance used in accordance with a sanction or approval granted" under the act, the Meat Inspection Act, or the Poultry Products Inspection Act before the enactment of the Food Additives Amendment of 1958. This type of sanction or approval is generally referred to as a "prior sanction." Neither the act nor its legislative history defines the term "prior sanction." However, FDA has adopted a regulation (21 CFR 170.3(l)) that defines this term as "an explicit approval granted with respect to use of a substance in food prior to September 6, 1958 * * *" under any of the three statutes listed above. Another FDA regulation (21 CFR 181.5(a)) states that a prior sanction "shall exist only for a specific use(s) of a substance in food, i.e., the level(s), condition(s), product(s), etc., for which there was explicit approval * * *."

The "explicit approval" required to establish a prior sanction may be either formal or informal. In the event that a formal approval, such as a food standard regulation promulgated under the act before 1958, does not exist, the agency recognizes that correspondence issued by authorized agency officials can constitute an informal prior sanction.

FDA has tentatively acknowledged "prior sanctions" for a number of specific uses of sulfiting agents in food. In the 1982 proposal, the agency noted several prior sanctions that allow the use of sodium sulfite and sulfur dioxide at levels of 200 to 300 ppm in molasses, dried fruits, and foods that are not good sources of vitamin B_1 (thiamine). In that proposal, the agency also stated that sodium bisulfite solution is prior-sanctioned for use as a dip to prevent darkening of fresh-peeled, uncooked potatoes, and that sodium bisulfite is also prior-sanctioned as a dip to control the incidence of black spot on shrimp (Ref. 1). For uses of sulfites different from those proposed as GRAS in the 1982 proposal, the agency requested any person intending to rely on a prior sanction to submit proof of its existence.

On November 13, 1985, the Grocery Manufacturers of America (GMA) submitted to the agency a report entitled "Documentation of Explicit Prior Sanctions for the Specific Use of Sulfites as Preservatives in Food and for Other Particular Food Uses" (the GMA Report) (Ref. 56). This report states that a prior sanction exists for the use of sulfites as preservatives in food, except in meat and in foods that are good sources of vitamin B_1, and thus that such use is exempt from regulation under the food additive provisions of the act.

The GMA report also claims that "[p]articular prior sanctions also exist for the use of sulfites in a number of specific food categories." The GMA report states that FDA sanctioned the use of sulfites as preservatives in dehydrated potato products, beverages, citrus fruit products, dehydrated fruits and vegetables, fresh fruits and vegetables, soft drinks, and other foods. The report states also that FDA sanctioned the use of sodium bisulfite and sodium sulfite to prevent the discoloration of, and to preserve, precut peeled potatoes. The report states that other prior sanctions exist for particular uses of sulfites in cherries, bakery products, beer and malt beverages, corn products, dough, gelatin, molasses, mushrooms, onion and garlic products, coconut, pickles and pickled vegetables, sauerkraut and horseradish, shrimp, syrups, wine, and wine vinegar.

Although GMA has claimed that there is a prior sanction for the use of sulfites on fresh fruits and vegetables, in an earlier rulemaking (51 FR 25021) the agency determined that this use of sulfiting agents may render the food injurious to health and thus adulterated under section 402(a)(1) of the act. Therefore, the agency has revoked the prior sanction for this use. GMA's claims with respect to prior sanctions for the use of sulfites on certain types of potatoes and potato products are under consideration in another rulemaking (52 FR 46968).

Many of the other prior sanctions claimed by GMA are for uses of sulfites

that FDA is proposing to affirm as GRAS in this document. For these uses, FDA is establishing specific limitations on the amount of residual sulfite that may be present in finished foods. In some cases, the limitations proposed in this document are less stringent (that is, permit a higher level of sulfites in certain finished foods) than those that GMA asserts are prior sanctioned. In these cases, the agency believes that there is no reason to acknowledge the prior sanctions that do exist by separate regulation. In a few cases, the limitations stated in this rulemaking are more stringent than those under the claimed prior sanctions in the GMA report, consistent with current good manufacturing practices and the range of levels reported now in use for various food products. Also, certain of the prior sanctions that GMA listed in its report are for uses of sulfites in food categories that were not considered or catalogued by the Panel because of the absence of data on the particular use. The agency discusses the status of these claimed prior sanctions in Section VII.B. of this preamble.

In addition to GMA's report, the agency has received two citizen petitions requesting that the agency recognize prior sanctions for the use of sulfites in maraschino cherries and glacé fruit and in beer and other malt beverages. The former petition (FAP 6CP3941), submitted by the Maraschino Cherry and Glacé Fruit Processors Association, was filed on May 16, 1986. The latter petition (FAP 6CP3960), submitted by the Beer Institute, was filed on July 30, 1986. The agency will respond to these two petitions in Section VII.B. below.

III. Summary of the Panel's Report on All Uses of Sulfites

On January 31, 1985, the Panel released its final report entitled "The Reexamination of the GRAS Status of Sulfiting Agents" (Ref. 6). That report provides the most recent, complete, and authoritative compilation of scientific information available about the use of sulfiting agents on food. It contains a thorough review of estimated levels of human exposure to sulfiting agents from a variety of food categories. It also contains a review of biological information relevant to sulfite exposure, including data from toxicological studies as well as clinical data relating to hypersensitivity reactions in humans. The report provides conclusions with respect to the GRAS status of the use of sulfiting agents in food. Those conclusions form a basis for FDA's tentative GRAS determinations in this document.

A. Exposure of Humans to Sulfiting Agents Used in Food

To estimate the per capita daily food intake of sulfites in the United States, the Panel used three basic types of information: (1) The amount of the ingredient present in various components of a diet at the time of consumption; (2) the kinds of foods in the daily diet and the frequency with which each is consumed; and (3) the average portion size for the various foods consumed. To obtain this information the Panel used data from the following sources: (1) "The 1977 Survey of Industry on the Use of Food Additives" by the National Research Council (Ref. 5); (2) information provided to FDA by the food industry in response to FDA's proposed rule in 1982 on the GRAS status of sulfites (Ref. 1); (3) the 1977–1978 National Food Consumption Survey of the U.S. Department of Agriculture (USDA) (Refs. 13, 14, and 15); (4) Agricultural Statistics (Ref. 16) and other USDA statistical publications (Refs. 17 and 18); and (5) "U.S. Imports for Consumption and General Imports" (Ref. 19). The Panel also gathered information from manufacturers and users of sulfiting agents.

From these sources the Panel created a table containing the following information: (1) Added and residual levels of sulfiting agents in processed foods; (2) estimated levels of sulfites in finished foods; (3) human intake of specific foods or categories of food; and (4) estimated per capita daily intake of sulfites (Ref. 6, Table 1). The table contains estimates of the daily intake of sulfites (measured as sulfur dioxide equivalents), in milligrams per person per day, from the following food categories for which data were available: baked goods and baking mixes, grain products, coffee and tea, condiments, dairy analogs, fish and seafood, fresh fruit, dried fruit, fruit juices, frozen fruit, canned fruit, fresh vegetables, canned vegetables, dried vegetables, frozen vegetables, vegetable juices, sugar, sweet sauces, jams and jellies, gravies and sauces, nonalcoholic beverages, alcoholic beverages, soups, gelatin, snack foods, protein isolates, and nut products.

The Panel noted several characteristics and problems in interpreting the exposure data in the table. The Panel pointed out that there is no relationship, necessarily, between "added" and "residual" levels of sulfites for a given food, because companies frequently reported values for either one or the other sulfite level but not both. The Panel also acknowledged that sulfites may be used in foods not included in the table. The Panel noted that it had contacted experts in food science and technology in USDA, in universities, and in industry and industry associations and had also consulted the literature to resolve uncertainties in the data of the table.

The Panel reported, after considering the whole body of exposure data available to it, as well as the associated uncertainties in those data, that the total per capita daily intake of sulfites from food is about 6 milligrams, as measured in "sulfur dioxide equivalents." The Panel stated that beer provides an additional 0.4 milligram per capita per day. It found some uncertainty with regard to the sulfite intake from wine. Based on the national food consumption survey intake data (Ref. 6, p. 28), the Panel found that wine provides an additional 0.8 milligrams per capita per day, but that it provides 3.7 milligrams per capita per day if one relies on the total quantity of wine distributed. Thus, the Panel found that it was reasonable to conclude that the mean daily intake of sulfur dioxide equivalents from food, wine, and beer does not exceed 10 milligrams (0.17 milligram per kilogram body weight for a 60-kilogram person).

For those individuals who consume wine or beer or both regularly, the Panel noted that there would be an additional 30 milligrams of sulfur dioxide equivalents for each 200 milliliters of wine and 10 milligrams for each liter of beer consumed. In comparison, the Codex Alimentarius Commission estimated in 1975 that heavy consumers of foods and beverages containing high levels of sulfites (99th percentile consumption) might have a daily intake of 177 milligrams sulfur dioxide equivalents (Ref. 6).

After consideration of all the data, the Panel concluded that the 99th percentile intake, including regular consumption of wine and beer, probably does not exceed 180 milligrams of sulfur dioxide equivalents per day (3 milligrams per kilogram body weight per day).

Thus, in summary, the Panel concluded that the mean daily intake of sulfites does not exceed 0.17 milligram per kilogram of body weight per day, and the 99th percentile intake does not exceed 3 milligrams per kilogram of body weight per day.

B. Biological Studies

The Panel reviewed in detail studies completed since the original 1976 evaluation of the GRAS status of sulfites conducted by the Select Committee. The information the Panel reviewed included studies on the metabolism and

metabolic effects of sulfites, short-term and long-term toxicity studies, teratogenicity studies, and mutagenicity and carcinogenicity studies. The Panel also reviewed clinical data and other information on sulfite sensitivity reactions that may occur when asthmatics or other sulfite-sensitive individuals ingest foods or beverages containing sulfites, inhale sulfur dioxide, or are given medications containing sulfites. That review of sulfite-sensitivity reactions was referenced in the agency's previous rulemakings concerning the use of sulfites on fresh fruits and vegetables and on "fresh" potatoes (Refs. 9 and 10). For that reason it will not be repeated here but is incorporated by reference (see, e.g., 50 FR 32830; 51 FR 25021; and 52 FR 46968).

1. Metabolism of Sulfites

Based on information it reviewed on the metabolism of sulfites, the Panel found that virtually all consumed sulfite is metabolized by sulfite oxidase in the mitochondria of various organs and tissues at a rate that is probably diffusion limited. The Panel stated that:

> The amount of endogenous sulfite is several orders of magnitude greater than that normally obtained from exogenous sources. Except for the few individuals identified as having congenital sulfite oxidase deficiency, it would appear that most individuals have sufficient enzyme to metabolize both endogenous and exogenous sulfite. Whether sulfite oxidase-deficient patients are sulfite sensitive as well remains to be established.

The Panel stated that "there is sufficient information in the current literature to conclude that some individuals, or a select subpopulation with a congenital deficiency of sulfite oxidase activity, would metabolize sulfite more slowly and may be subject to adverse effects from sulfite at the current level of intake." The Panel concluded, however, that there is "no reason to presume that individuals with the usual levels of sulfite oxidase activity and adequate nutritional status should develop adverse health effects from consumption of sulfite in foods at the levels currently used."

2. Toxicity Studies on Sulfites

The Panel was unable to locate any animal feeding studies on the acute oral toxicity of sulfiting agents published after 1976. Acute exposure seems to be a factor in sensitivity reactions associated with ingestion of foods or beverages containing sulfiting agents, but sensitivity reactions appear to be separate and distinct from other manifestations of acute oral toxicity. Feron and Wensvoort (Ref. 20) and Til et al. (Refs. 21 and 22) reported gastric lesions in several chronic feeding studies published before 1976. In one study by Beems et al. (Ref. 23), the types of gastric lesions induced by feeding sodium metabisulfite to Wistar Random rats were examined by enzyme histochemistry and light and electron microscopy. Animals were fed thiamine-supplemented diets containing 0, 4, and 6 percent sodium metabisulfite for 4, 7, 14, 21, or 28 days in a time-sequence study. Fundic mucosa of the rats fed sodium metabisulfite contained scattered hyperplastic glands lined with enlarged hyperactive gastric chief cells containing large numbers of pepsinogen granules but no fat, glycogen, or mucus. Findings from the time-sequence study suggested that preexisting chief cells were transformed to hyperactive chief cells having proliferative capabilities.

Gunnison et al. examined the subchronic toxicity of sulfite in female rats with low levels of sulfite oxidase activity that had been induced by their being fed low molybdenum diets, which contained tungstate, for 9 weeks (Ref. 24). Beginning on day 21, drinking water for two groups of animals also included 25 or 50 millimolar of sulfite ($SO_3^{=}$). This treatment resulted in levels of hepatic sulfite oxidase activity 1 percent of that in untreated rats and 10 percent of that in normal humans. The authors reported that the general health of the rats appeared normal, and that the differences in weight gains and organ weights of pregnant and nonpregnant animals were not correlated with exogenous sulfite levels. Nonpregnant animals given sulfite did not develop anemia, and hematologic measurements in pregnant animals showed changes normally associated with pregnancy. Erythrocyte glutathione concentrations and prothrombin times were not affected, and hepatic thiamine concentrations were not significantly reduced by administration of sulfite to rats with low levels of sulfite oxidase activity. S-sulfonate concentrations in aorta pinna, and plasma were elevated in animals with low levels of sulfite oxidase activity. Administration of sulfite produced additional increments in S-sulfonate levels in aorta. Trends appeared similar, but data were incomplete for pinna and plasma concentrations of S-sulfonates.

With regard to short- and long-term toxicity studies, the Panel concurred with the conclusion of the Select Committee (Ref. 2) concerning the "no-observed-adverse-effect level" of sulfiting agents for chronic toxic effects. The Select Committee concluded that the level of sulfite that produces no observed toxic effects varies from about 30 to 100 milligrams of sulfur dioxide per kilogram of body weight per day, depending on the species and experimental conditions.

The Panel stated that it had not found any new data that was inconsistent with the data considered earlier by the Select Committee. Moreover, the Panel stated that it is evident from examination of experimental protocols that the no-observed-adverse-chronic-effect level is probably nearer the upper portion of the range (100 milligrams sulfur dioxide) than the lower portion of the range (30 milligrams sulfur dioxide).

3. Teratogenicity Studies on Sulfites

Dulak et al. studied the reproductive performance of female Wistar-derived rats that had induced sulfite oxidase deficiency and that were exposed to 25 or 50 millimolar sulfite (160 or 280 milligrams per kilogram of body weight per day) as sodium metabisulfite in drinking water from 3 weeks before mating until day 20 of gestation (Ref. 25). No treatment-related trends in reproductive performance or malformations were reported after animals having deficient or normal levels of sulfite oxidase activity were exposed to sulfite.

In a study by Murray et al., inhalation of sulfur dioxide in filtered room air for 7 hours per day by CF-1 mice (25 ppm on days 6 through 15 of gestation) and New Zealand rabbits (70 ppm on days 6 through 18 of gestation) resulted in no evidence of maternal toxicity except for decreased food consumption by both species during the first few days of exposure (Ref. 26). An increase in minor skeletal variants in both species was associated with maternal exposure to sulfur dioxide, but no teratogenic effects were observed in either species (Ref. 26).

It was the opinion of the Panel that the available data, including the studies considered by the 1976 Select Committee, do not provide evidence that sulfiting agents have teratogenic effects.

4. Mutagenicity and Carcinogenicity Studies on Sulfites

The Panel noted that Shapiro has reported that bisulfite (10 millimolar; pH not specified) induced mutations in *Staphylococcus aureus*, and that bisulfite (5 millimolar) induced mutations at pH 3.6 but not pH 5.5 in *Saccharomyces cerevisiae* (Ref. 27). Mallon and Rossman reported that bisulfite (0.1 molar) did not cause mutations in *Escherichia coli* (Ref. 28). Khoudokormoff and Gist-Brocades reported in 1978 that, in a *Bacillus subtilis* test system, concentrations of sulfur dioxide similar to those found in

wines (150 ppm, pH 3.0 to 6.5) did not elicit any mutagenic activity (Ref. 29). Also Chang et al. have reported that, in a *B. subtilis* test system, higher concentrations of a sodium sulfite-bisulfite mixture (0.1 molar to 0.5 molar; pH 7) showed mutagenic effects, whereas a lower concentration of this mixture (0.05 molar; pH 7) caused no mutagenic activity. Cells treated with adducts of sodium bisulfite and cytidine monophosphate or uridine monophosphate showed mutagenic effects at concentrations of 0.25 molar and 0.5 molar (Ref. 30).

DiPaolo et al. have reported that transformation of Syrian hamster embryo cells treated with 1, 5, or 10 millimolar bisulfite for 24 hours at neutral pH was increased in a dose-dependent fashion (Ref. 31a). These authors suggested, however, that this transformation might not occur by a mutagenic mechanism because bisulfite in combination with ultraviolet irradiation did not synergistically increase transformation. Further work by Doniger et al. in this system indicated that bisulfite caused no detectable deoxyribonucleic acid (DNA) damage and may have decreased the rate of DNA replication per cell by blocking operation of part of the functioning replicons (Ref. 31b). MacRae and Stich reported that in Chinese hamster ovary cells, dose- and time-dependent inductions of sister chromatid exchange were seen following exposure to 0.03 millimolar to 7.3 millimolar concentrations of bisulfite for 2 or 24 hours (Ref. 32).

In contrast, Mallon and Rossman have demonstrated that Chinese hamster cells exposed for 15 minutes to 10 and 20 millimolar bisulfite exhibited no mutations to ouabain resistance (Ref. 28). Likewise, exposure for 15 minutes to 10 millimolar bisulfite produced no mutations to 6-thioguanine resistance. Long-term exposure of Chinese hamster V79 cells (exposed continually and recultured for 8 weeks in a complete growth medium containing 5 millimolar bisulfite) also failed to induce ouabain resistant mutations (Ref. 28). According to Schneider and Calkins, cultures of lymphocytes from human peripheral blood exhibited chromosomal abnormalities (clumping) and decreases in DNA synthesis, cell growth, and mitotic indices after a single exposure to 100 milliliters of 5.7 ppm sulfur dioxide in air on day 0 or day 1 of incubation but not on day 2 or day 3 (Ref. 33).

While chromosomal aberrations have been observed in response to sulfites in in vitro systems, mutagenic effects have not been reported in intact animals exposed to sulfur dioxide or sulfites. Generoso et al. have reported the dominant-lethal mutations were not increased in 10- to 12-week-old (C3H x 101) F_1 female mice given one intraperitoneal injection of 550 milligrams per kilogram of sodium bisulfite and mated with untreated (101 x C3H) F_1 males within 4.5 days of treatment (Ref. 34). In the same study, neither heritable translocations nor dominant-lethal mutations were detected when (101 x C3H) F_1 male mice were mated with (C3H x C57BL) F_1 females after intraperitoneal injections of 400 milligrams per kilogram of sodium bisulfite 20 times during a 26-day period or of 300 milligrams per kilogram 38 times during a 54-day period.

Jagiello et al. reported that chromosomal aberrations were not found in oocytes of female Camm mice given one intravenous injection of 1.0, 2.5, or 5.0 milligrams sodium sulfite although structural damage was reported during meiosis when cultures of Camm mouse oocytes were treated with sodium sulfite (Ref. 35). Renner and Wever have reported that no cytogenetic effects (measured by sister chromatid exchange, chromosomal aberration, and micronucleus tests) were induced in bone marrow cells of either Chinese hamsters or NMRI mice (made sulfite oxidase-deficient by feeding a low molybdenum diet plus administration of sodium tungstate in drinking water) in response to subcutaneous or intraperitoneal injection or oral administration of sodium metabisulfite solution (Ref. 36). However, the authors noted that the control animals tolerated higher doses of sulfite than those made sulfite oxidase-deficient (Ref. 36).

According to Tanaka et al., male and female ICR/JCL mice administered 1 and 2 percent potassium metabisulfite in drinking water for 24 months had no increased incidence of tumors over control animals, suggesting that potassium metabisulfite is not carcinogenic in mice (Ref. 37). Peacock and Spence have reported that exposure to sulfur dioxide by inhalation was associated with an increase in lung tumors, but the increase was not statistically significant (Ref. 38). According to Laskin et al., inhalation of sulfur dioxide in combination with benz(a)pyrene resulted in an increased incidence of tumors in rats over exposure to either substance alone. Rats exposed only to sulfur dioxide had no tumors at the end of the experimental period (Ref. 39).

Gunnison et al. reported an unexpected finding of mammary adenocarcinomas after 9 weeks of treatment in 4 of 149 female rats (2 pregnant, 2 nonpregnant) with low activity of sulfite oxidase induced by a low molybdenum diet containing tungstate. No tumors were found in rats with normal levels of sulfite oxidase activity. The difference was not statistically significant (Ref. 24).

Two Swedish studies examined the effects of sulfur dioxide on the peripheral blood cells of workers that were exposed to this substance. Nordenson et al. observed an increase in chromosomal aberrations (mostly gaps and chromatid-type breaks) in 7 of 19 workers who were exposed to other inhalants as well in a sulfite pulp factory (Ref. 40). However, Sorsa et al. observed that peripheral blood lymphocytes of eight workers whose individual mean daily exposure to sulfur dioxide in an aluminum foundry was estimated to be 1.0 ± 0.85 ppm had no greater incidence of chromosomal aberrations or sister chromatid exchange than eight age-control subjects (Ref. 41). Average daily sulfur dioxide exposures in the aluminum foundry were estimated to range from 0.2 to 3.0 ppm., and mean employment time for the exposed workers was 19.5 years (Ref. 41).

The Panel noted that possible synergistic effects of sulfur dioxide and sulfites with other compounds have been examined in an effort to determine whether sulfiting agents might act as comutagens or cocarcinogens. Mallon and Rossman reported that mutation frequency was approximately doubled in ultraviolet-irradiated Chinese hamster cells exposed to 10 millimolar bisulfite either during or after irradiation exposure, and tryptophan revertants were increased by more than eightfold in ultraviolet-treated *E. coli* cells exposed to 75 millimolar bisulfite (Ref. 28). Hayatsu and Kitajo reported that treatment of bacteriophage-*lambda* with bisulfite-amine mixtures (1 molar bisulfite plus 1 molar semicarbazide, hydrazine, methoxyamine, or hydroxylamine) produced increases in clear mutation (plaque-forming activity) over treatment with bisulfite alone (Ref. 42). Khoudokormoff and Gist-Brocades reported that combination of bisulfite (150 ppm) with nitrite (100, 200, or 400 ppm) produced a weak mutagenic effect after 2 weeks in *B. subtilis* (Ref 29). Suwa et al. reported that mutagenic effects of coffee on *Samonella typhimurium* strains TA 100 and TA 98 without S9 mix were completely inhibited by addition of 300 ppm sulfiting agents (sulfite, bisulfite, or metabisulfite), and phage-inducing

activity of coffee (prophage-*lambda* induction test) was suppresed by 300 ppm sulfite ion (Ref. 43). Sodium sulfite was also noted by Calle and Sullivan to be a weak inhibitor of mutagenic effects induced by benz(a)pyrene in *S. typhimurium* strain TA 98 (Ref. 44). Borek reported that bisulfite concentrations relevant to use in foods (0.5, 2.5, and 5.0 micrograms per milliliter), as well as a higher concentration of 100 milligrams per milliliter, inhibited transformation of C_3H 10T 1/2 cells by x-rays and benz(a)pyrene. Pretreatment of hamster embryo cells with 100 ppm bisulfite inhibited transformation by x-rays (Refs. 45 and 46).

With respect to the mutagenicity or carcinogenicity potential of sulfites, the Panel concluded, upon consideration of the new studies, as well as the data available to the Select Committee in 1976, that sulfites are mutagenic to several microorganisms and may produce chromosome damage to mammalian cells in vitro. Sulfites, however, also inhibit mutagenic effects of some known mutagens and carcinogens. The Panel concluded that sulfites are not carcinogenic or mutagenic in vivo to rats and mice.

C. Conclusions and Recommendations of the Panel

In summary, the Panel concluded that sulfiting agents are not teratogenic, mutagenic, or carcinogenic in laboratory animals. The Panel found no new metabolic or toxicological data in its review of sulfiting agents that suggest a need to change the no-observed-adverse-effect level for sulfites and stated that an examination of exposure and consumption data indicates that the level of consumption of sulfites from foods and beverages is about the same as that estimated by the Select Committee in 1976.

The Panel further compared the no-observed-adverse-effect level from chronic toxicity studies to the likely upper limit levels of human intake (found by the Panel to range from a mean of less than 0.17 milligram per kilogram of body weight per day to a 99th percentile value of less than 3 milligrams per kilogram of body weight per day). The Panel compared these intake levels to the no-observed-adverse-effect levels based on animal toxicity data (estimated to range from 30 milligrams to 100 milligrams sulfur dioxide equivalents per kilogram of body weight per day). The Panel determined that the margin between the amount of sulfur dioxide equivalents ingested by high intake consumers and the lowest estimated no-observed-adverse-effect level is about tenfold (30 milligrams per kilogram of body weight per day divided by 3 milligrams per kilogram of body weight per day). The Panel concluded that the margin between the mean per capita daily intake and the lowest no-observed-adverse-effect level is about 180-fold (30 milligrams per kilogram of body weight per day divided by 0.17 milligram per kilogram of body weight per day). The Panel noted that "consideration of the significance of this difference should recognize the difficulties in estimating with confidence the components which are the basis of the calculated safety margin." (Ref. 6.)

The Panel found that none of the five traditional conclusion statements (Ref. 3) considered by the Select Committee on GRAS Substances for its 1976 report is appropriate for sulfites. The Panel's conclusion statement for sulfites contains two parts. The Panel first concluded that:

> For the majority of the population, there is no evidence in the available information on potassium bisulfite, potassium metabisulfite, sodium bisulfite, sodium metabisulfite, sodium sulfite, and sulfur dioxide that demonstrates or suggests reasonable grounds to suspect a hazard to the public when these substances are used at levels that are now current and in the manner now practices. However, it is not possible to determine, without additional data, whether a significant increase in consumption would constitute a dietary hazard.

Second, the Panel concluded that:

> For the fraction of the public that is sulfite sensitive, there is evidence in the available information on potassium bisulfite, potassium metabisulfite, sodium bisulfite, sodium metabisulfite, sodium sulfite, and sulfur dioxide that demonstrates or suggests reasonable grounds to suspect a hazard of unpredictable severity to such individuals when they are exposed to sulfiting agents in some foods at levels that are now current and in the manner now practiced.

IV. FDA's Evaluation of the Panel's Report

FDA has undertaken its own evaluation of the data that formed the basis for the Panel's report. The agency has evaluated the report's human exposure estimates, estimates of highest no-observed-adverse-effect level for sulfites, its estimates of safety margins (ratios of no-observed-adverse-effect levels to human exposure values) for the use of sulfites in human food, and the Panel's overall conclusions.

A. Exposure Estimates

The Panel determined that the mean human intake of sulfites from food does not exceed 0.17 milligram per kilogram of body weight per day (sulfur dioxide equivalents), and that intake from a hypothetical meal high in sulfited foods, which includes consumption of wine and beer, does not exceed 3 milligrams per kilogram of body weight per day (sulfur dioxide equivalents). The agency has reviewed the data and the Panel's estimates and has estimated that the mean level of chronic intake of sulfiting agents does not exceed 0.3 milligram per kilogram of body weight per day (sulfur dioxide equivalents), a figure slightly higher than the Panel's estimate.

The agency also used data from the Panel's report and from the National Food Consumption Survey "Foods Commonly Eaten by Individuals" (Ref. 13), combined with typical sulfur dioxide equivalent residues, to compute an acute 99th percentile intake of sulfites based on a single eating occasion of highly sulfited foods. The agency did not include exposure to sulfites from their use on fresh fruits and vegetables in this computation (or in its computation of mean chronic intake). Based on its computation, FDA would not expect this 99th percentile intake of sulfites to exceed approximately 5 milligrams per kilogram body weight per day.

Even though the information bases available to the agency and to the Panel were virtually the same, the agency's estimates are somewhat different from the Panel's because the agency used some different assumptions in its calculations. The agency's estimates differed from those of the Panel in two ways: (1) use of market share factors, and (2) selection of typical sulfur dioxide equivalent residue levels.

Market share factors are estimated percentages of the foods in each of the dietary food categories listed in 21 CFR 170.3(n) that may contain the additive. Such market share factors are applied to adjust intake estimates to reflect actual usage of an ingredient based on economic and technological considerations. For example, current information indicates that sulfite-treated flour is useful in only certain types of products within the dietary food category "Baked Good," such as pie crusts, crackers, and cookies. Consequently, FDA adjusted its estimate of exposure to sulfites from this food category to reflect this fact. The agency found, however, that the Panel did not apply market share factors in reaching its exposure estimates.

The agency also selected a different typical sulfur dioxide equivalent residue level for certain food uses than did the Panel. In reviewing the available information, the agency determined that the Panel sometimes used a sulfur

dioxide equivalent residue value that was derived from an opinion expressed by food industry representatives. The agency, however, gave the greatest weight to sulfur dioxide equivalent residue values that were derived from actual analyses of food and consideration of whether the analyzed samples were representative. Information gathered for the Panel's review aided the agency in refining its estimates of sulfite intake. However, the new result of these different procedures was different estimates of sulfur dioxide equivalent intake between the Panel and the agency.

The exposure estimates provided by the Panel and reevaluated by the agency, i.e., the mean intake levels and the intake level of the hypothetical high consumer of sulfited foods including the consumption of wine and beer, include within their range the 90th percentile intake level, the level that the agency has traditionally used in the safety evaluation of numerous food ingredients. In fact, the Panel, which examined 1977 data on sulfites from the National Academy of Sciences (NAS) (Ref. 5), estimated the 90th percentile intake, including the consumption of wine and beer, to be 43 milligrams per day (0.72 milligram per kilogram per day). The Panel estimated the mean intake level for a consumer, including the consumption of wine and beer, to be 19 milligrams per day (0.32 milligram per kilogram per day) (Ref. 6, p. 25). Therefore, the 90th percentile intake can be expected to exceed the mean intake by approximately a factor of 2.3 (0.72 as compared to 0.32 milligram per kilogram per day).

B. Estimates of Highers No-Observed-Adverse-Effect Levels for Sulfites

The Panel estimated that the no-observed-adverse-effect level for sulfites ranged from 30 milligrams per kilogram of body weight per day (sulfur dioxide equivalent) to 100 milligrams per kilogram of body weight per day (sulfur dioxide equivalent) and was probably closer to the value of 100 milligrams per kilogram of body weight per day (Ref. 6, pp. 42 and 58).

The agency has reviewed the available data and the Panel's conclusions on the toxicology of sulfiting agents. In its review, the agency found no data that would cause it to disagree with the Panel that the no-observed-adverse-effect level for sulfites is in the range of 30 to 100 milligrams per kilogram of body weight per day (sulfur dioxide equivalents).

C. Safety Margin for Sulfites

The agency normally establishes the safety of new food additives by applying a safety factor to the no-observed-adverse-effect level for the ingredient. Traditionally, the agency has determined the maximum acceptable daily human intake of the food additive (in units of milligrams per kilogram of body weight per day) by multiplying the no-observed-adverse-effect level from chronic animal experimentation data by the safety factor of 1/100 as provided in the agency's regulations for food additives in 21 CFR 170.22. For any food ingredient that is currently in use, one may compute the current safety margin by determining the ratio of the no-observed-adverse-effect level from chronic animal experimentation data (in milligrams per kilogram of body weight per day) to the chronic estimated daily human intake of the ingredient (in milligrams per kilogram of body weight per day).

Using the lowest (most conservative) of the no-observed-adverse-effect level values (30 milligrams per kilogram of body weight per day), the agency calculates that the safety margin is approximately 100 for the estimated chronic mean intake of sulfites (30 milligrams per kilogram of body weight per day) divided by (0.3 milligram per kilogram of body weight per day). This margin is consistent with the safety factor that the agency, in most circumstances, applies to new food additives.

The agency also notes that acute sulfite intake that results from infrequent ingestion of meals containing a number of highly sulfited foods is not representative of the food intake patterns that lead to the development of chronic conditions, and it is not valid to compare such intakes to the no-observed-adverse-effect level obtained from a chronic feeding study to derive a safety margin. The concerns presented by such extreme eating patterns are not related to chronic toxic effects but rather have a bearing on acute sulfite-sensitivity reactions. As noted above, the adverse health consequences of acute high intake of sulfites in humans have been characterized in clinical studies, and the agency has addressed the public health concerns arising from such acute intakes in separate rulemakings.

For a new food additive for which there is not yet an approval, the agency traditionally has used a 90th percentile chronic exposure estimate to calculate the safety margin. A 90th percentile exposure value was not calculated for sulfiting agents from the most recent data. For the purposes of this discussion, however, the agency has calculated a 90th percentile value. Using the National Academy of Sciences data discussed above, the agency has calculated the 90th percentile to be at least two times greater than the mean. Multiplying the mean by two yields as estimated value of 36 milligrams per day (0.6 milligram per kilogram per day) sulfites for the daily intake of sulfites at the 90th percentile.

The agency believes, based on its review of the toxicity data on sulfites, that the true no-observed-adverse-effect level is approximately 100 milligrams per kilogram per day, consistent with the findings of the Panel (Ref. 6, pp. 42 and 58). Based on these considerations, the agency calculates a safety factor of 170 (100 milligrams per kilogram per day divided by 0.6 milligram per kilogram per day) for the calculated 90th percentile intake value, and a safety factor of 340 for the chronic intake. Therefore, the agency believes that an adequate margin of safety does exist between the no-observed-adverse-effect level for sulfites and chronic mean intake and estimated 90th percentile intake of individuals.

D. The Panel's Conclusion

The agency had reviewed the Panel's two-part conclusion. The first part of the conclusion was directed at the GRAS status of most uses of sulfites and was concerned with exposure of the vast majority of consumers. The second part was directed at that subpopulation of consumers that are sensitive to sulfites, especially when the sulfites are used on certain categories of foods.

The agency has already responded to the latter conclusion in the final rule on the use of sulfiting agents on fresh fruits and vegetables and in the proposal on potatoes (Refs. 9 and 10). With respect to the GRAS status of the overall use of sulfites on food (the first element of the Panel's conclusion), the Panel concluded that, except for certain exposures of the subpopulation of individuals sensitive to sulfites, the use of these ingredients on food in GRAS.

On the basis of its review of all available information, the agency has not found any reasons to disagree with the Panel's conclusions.

V. The Advisory Committee on Hypersensitivity to Food Constituents

In the **Federal Register** of April 16, 1984 (49 FR 15021), FDA announced that the Secretary of the Department of Health and Human Services established an ad hoc Advisory Committee on Hypersensitivity to Sulfiting Agents in

Foods (later renamed the Advisory Committee on Hypersensitivity to Food Constituents) to function under FDA's Center for Food Safety and Applied Nutrition. The Committee reviewed and evaluated available information and data relevant to the allergic-type responses in humans that are associated with food ingredients, including sulfiting agents, for the purpose of making appropriate recommendations to the Commissioner of Food and Drugs.

The Committee met on December 12 and 13, 1985, to review specifically the available information on the use of sulfiting agents in food. The Committee generally supported FDA's proposal to rescind the GRAS status of the use of sulfites on fresh fruits and vegetables (Ref. 9a), and encouraged FDA to include "fresh potatoes" in this section (Ref. 47).

VI. Comments

Even though the extended comment period closed on December 7, 1982, the agency has continued to receive comments regarding sulfiting agents. The agency has received comments from consumers, consumer groups, Congressional representatives on behalf of consumers, health professionals and scientists, Federal, State, and local government officials, the food industry, and industry trade associations.

Many comments received since 1982 pertained to alleged adverse effects experienced by consumers who consumed foods, particularly fresh fruits and vegetables and potatoes or potato products, that were treated with sulfites. Among the comments received from consumers, approximatley 38 percent were reports of alleged adverse reactions to sulfiting agents in food. Other consumer comments recommended various courses of action: Roughly 27 percent urged the agency to ban sulfites from all use in foods. About 1.5 percent suggested a ban on certain uses of sulfites in certain foods, and a similar proportion (about 1.5 percent) requested that limits be placed on the use of sulfites in food. Over 15 percent of the comments received from consumers advocated the use of labeling on foods containing sulfiting agents, and a similar proportion (about 15 percent) expressed a general concern about the use of sulfites in food.

FDA has responded to comments that relate to adverse reactions by sulfite-sensitive persons, or to the use of sulfites on fresh fruits and vegetables and on potatoes or potato products, in previously published **Federal Register** documents (Refs. 9 and 10). In this document, the agency will respond only to those comments that pertain to the overall GRAS status of sulfites in food and to the GRAS status of those uses of sulfites that have not already been addressed by the agency.

On October 28, 1982, the agency received a citizen petition regarding sulfiting agents in food and drugs. (The petitioner supplemented the petition on March 15, 1983, August 17, 1983, and July 25, 1986.) The agency's response to those aspects of the citizen petition that relate to the use of sulfites on food is presented in section VI.B. below.

A. General Comments

Two comments from industry sources supported the 1982 proposal as written. The remaining comments from industry presented information in support of modifications in the proposal. Most industry comments requested GRAS affirmation for uses of sulfiting agents, including uses of sodium sulfite that were previously unreported and that were consequently not considered by the Select Committee. Many comments also requested modifications with regard to some of the reported uses, including higher or lower sulfite treatment levels in foods, additional technical effects, use of residual sulfur dioxide levels instead of treatment levels, or deletion of all use limitations. Some comments presented information that, according to the comments, demonstrated that any one of several sulfiting agents could be used to accomplish the same technical effect in a food product. These comments requested that the agency permit the interchangeable use of two or more of the sulfiting agents.

A number of comments reported information on the use levels or residual levels of various sulfiting agents in foods. Some provided data and information on sulfite sensitivity reactions. FDA gave a number of the comments to the Panel for consideration at the Panel's request.

1. Potassium Bisulfite and Sodium Sulfite

Numerous comments from industry and industry trade associations, in response to the July 9, 1982, proposal, requested that FDA not deny GRAS status to the use of potassium bisulfite and sodium sulfite. In the 1982 proposal, the agency said that it did not have any evidence of food use of potassium bisulfite, and that it did not have sufficient information relating to the food use of sodium sulfite to establish limitations on the use of this ingredient. FDA stated that as a result, it could not affirm these ingredients as GRAS. Instead, FDA proposed to remove these ingredients from the list of substances that are GRAS.

The comments described current uses of these two sulfiting agents in a variety of food products, demonstrating that they are, in fact, being used by industry. The agency considers that these comments have provided sufficient evidence of the use of sodium sulfite and potassium bisulfite to warrant affirming that the use of these ingredients is GRAS.

2. Interchangeable Use of Sulfiting Agents

A number of comments expressed the opinion that several sulfiting agents ought to be fully interchangeable. In particular, the comments noted the desirability of allowing food processors to substitute potassium salts of the sulfiting agents for sodium salts to reduce the sodium content of processed foods and thus to contribute to a reduction in the level of sodium consumption in the United States.

The agency has found no evidence that the six sulfiting agents that are the subject of this rulemaking are not fully interchangeable. In fact, interchangeability could offer manufacturers and food processors greater flexibility in formulating foods and could facilitate the substitution of potassium salts for sodium salts where feasible. Therefore, the agency is providing for the interchangeability of all sulfiting agents in this rulemaking by setting forth in the regulations maximum permitted residual levels of sulfites in food in terms of sulfur dioxide equivalents rather than in terms of any specific sulfiting agent.

As noted above, sulfur dioxide equivalents are a measure of the proportion of the sulfiting agent that can chemically dissociate into sulfur dioxide. Different sulfiting agents possess different percentages of sulfur dioxide per unit weight. The use of sulfur dioxide equivalents to measure the maximum permitted residual levels of sulfites in food correctly focuses on that portion of the sulfiting agent that is of biological significance, the sulfur dioxide, and not the parent chemical. As long as sulfur dioxide equivalents are used to measure the sulfite content of foods, sulfiting agents may be used interchangeably.

3. Claimed Inconsistencies in Proposal

One comment pointed out that the limitations on the use of sulfiting agents in the 1982 proposal were inconsistent. As an example, the comment cited the fact that the limitations on the use of two different sulfiting agents differed by

a factor of 100 in the same food categories. The comment stated that such an inconsistency would present problems for industry because it creates ambiguity.

The agency believes that this concern has been eliminated because the agency is permitting the sulfiting agents to be used interchangeably. This approach was explained in the response to the previous comment.

4. Levels of Use

A number of comments from segments of the food industry addressed specific use levels or residual levels of sulfiting agents in specific food products. Some comments argued for different treatment levels from certain sulfiting agents than those that the agency had specified in the July 1982 proposal. Some comments requested that limitations on sulfites be stated in terms of residual levels on the finished food product rather than in terms of treatment levels.

The agency believes that the most reasonable way to define limitations on sulfite use in food is to use the levels of sulfites on finished food products measured as sulfur dioxide equivalents. (A "finished food" is the product as manufactured.) The amount of sulfite present on a particular food at the time that it is consumed may differ from the amount remaining on that food just after processing. The latter amount of sulfite may, in turn, differ from the amount actually used to treat the unprocessed food. Such differences reflect the fact that a significant amount of applied sulfites can be lost from foods during processing, storage, distribution, or home preparation. These losses can result from either physical processes, such as volatilization, or chemical processes, which involve chemical reactions with food constituents. Because levels of sulfites in finished foods may differ considerably (and unpredictably) from treatment levels, and because finished foods are those most readily available to the agency for determining compliance, FDA has tentatively concluded that it does not make sense to base the specific limitations on the level of sulfites in the food at the time it is treated or at the time it is consumed.

The agency concludes that setting specific limitations on the level of residual sulfur dioxide equivalents in the finished food will most effectively ensure the safety of treated foods and will also allow compliance with the limitations to be more accurately verified. This approach is also the approach used in the recent rulemaking concerning the labeling of food products that contain sulfiting agents (Refs. 7 and 8).

5. Home Use of Sulfites

One comment submitted that sulfiting agents are currently being sold directly to the general public for use in home drying, freezing, and canning of fruits and vegetables. The comment expressed concern about the potential effects of sulfite regulations on the selling of sodium metabisulfite as an accessory to the home food dehydration equipment manufactured by the company that submitted the comment.

The agency notes that the direct marketing of sulfiting agents for home use was not reviewed or evaluated by the Select Committee or by the Panel. Thus, the agency believes that there is currently no basis for affirming the GRAS status of the home use of sulfiting agents for drying, freezing, canning fruits and vegetables, or for other uses, such as home winemaking. In fact, such uses of sulfites may present hazards to consumers who are sulfite sensitive. Sulfiting agents sold for home use might lack adequate directions for use or may by misused by the consumer. Thus, the possibility exists that sulfite-sensitive individuals may be unwittingly exposed to excessive levels of sulfites on food produced at home. Therefore, the agency cannot affirm the GRAS status of these uses of sulfiting agents.

The ad hoc Advisory Committee on Hypersensitivity to Food Constituents considered the use of sulfiting agents in home drying of foods during its December 12, 1985, meeting (Ref. 47, p. 368). At that time, the Advisory Committee voted unanimously to recommend "the banning of the sale of sulfites and formulated sulfite products for use as fruit and vegetable fresheners and potato whiteners at the retail and consumer level" (Ref. 47, p. 363). Given this recommendation, and given that the use of sulfites in home dehydration equipment and other home uses was not reviewed by the Panel, the agency tentatively concludes that there is insufficient information to affirm these uses of sulfites as GRAS, and solicits further comments and information on such uses.

6. Identification of Sulfur Dioxide and Sodium Metabisulfite

One comment requested that the agency adopt the specifications for sulfur dioxide in the 3d edition of the Food Chemicals Codex. Another comment requested that the agency adopt the Chemical Abstracts Service (CAS) registry number that is used by the Environmental Protection Agency for sodium metabisulfite.

The agency agrees that the specifications for sulfur dioxide, as with almost all direct food additives, should be those stated in the 3d edition of the Food Chemicals Codex. The present rulemaking reflects that fact. In addition, the agency has verified the latest CAS registry numbers for all sulfiting agents that are the subject of this rulemaking and is incorporating those numbers in the proposed GRAS affirmation regulation.

Furthermore, the agency is also proposing to adopt the specifications listed in the Food Chemicals Codex, 3d Ed., for potassium metabisulfite, sodium bisulfite, sodium metabisulfite, and sodium sulfite. However, no food-grade specifications exist for potassium bisulfite. The agency will work with the Committee on Food Chemicals Codex of the National Academy of Sciences to develop acceptable specifications for this ingredient. When acceptable specifications are developed, the agency will incorporate them into § 184.1861, should FDA decide to adopt this regulation. Until specifications are developed, FDA has determined that the public health will be adequately protected if potassium bisulfite complies with the description in the proposed regulation and is of food-grade purity (21 CFR 170.30(h)(1) and 182.1(b)(3)).

7. Description of Sodium Bisulfite

One comment submitted data to establish that the chemical description provided in the July 9, 1982, proposal for sodium bisulfite does not adequately describe the ingredient of commerce. This comment noted that sodium bisulfite is not available commercially in a pure dry powder form and exists only as an aqueous solution.

FDA is aware that the articles of commerce called "anhydrous sodium bisulfite" and "anhydrous potassium bisulfite" are, in reality, mixtures of the salts sodium bisulfite and sodium metabisulfite and of the salts potassium bisulfite and potassium metabisulfite, respectively. When added to water, these mixtures produce aqueous solutions of sodium bisulfite and of potassium bisulfite, respectively. Therefore, FDA is revising the description of both sodium and potassium bisulfite in this rulemaking to reflect the fact that certain of the articles of commerce that are subject to this rulemaking are mixtures of bisulfite and metabisulfite salts.

8. Wine Institute Comment

BATF has forwarded to FDA a comment and data on sulfites that it received from the Wine Institute. The

Wine Institute had originally submitted these data to BATF in a December 23, 1985, comment to BATF Notice No. 566 (Ref. 48), which proposed mandatory sulfite labeling for alcoholic beverages that contain sulfites. The Wine Institute comment stated that the Monier-Williams method for measuring the sulfur dioxide content of sulfite-treated foods is inaccurate because it makes no distinction between "free" and "bound" sulfites. (The Monier-Williams method is the analytical method adopted, with modifications, by the agency for detecting sulfite levels in food (Ref. 8).) The comment asserted that "bound" sulfites are not the cause of any perceived adverse reactions to sulfites in individuals. Therefore, the comment argued that measurement of the sulfite content of a food by the Monier-Williams method may produce an inaccurate measure of the risk to individuals from sulfites in that food. The Wine Institute included with its comment the results of a study of sulfite-sensitive individuals challenged with wine to which known quantities of "bound" sulfites had been added. The purpose of the study was to determine the extent to which "bound" sulfites in wine may cause significant adverse reactions in sulfite-sensitive individuals.

FDA has reviewed this comment and the data submitted with it. These data do not present sufficient evidence to justify a change in the agency's belief that both types of sulfites may be potential sources of risk for sulfite-sensitive persons. As noted in the preamble to the final rule on labeling requirements for sulfiting agents (51 FR 25012), the agency has also received data indicating that bound sulfites may contribute to adverse reactions in humans. The agency believes that the available data do not resolve the question of whether "bound," as opposed to "free," sulfites in food can be responsible for adverse reactions in sulfite-sensitive individuals. Until more conclusive data become available, the agency cannot distinguish between "bound" and "free" sulfites in food and will continue to rely on the modified Monier-Williams analytical method for the quantitative detection of total sulfites.

FDA selected this method because it measures the free sulfite plus a reproducible portion of the bound sulfites, such as the carbonyl addition products, in the food. While it may be preferable to have a method that would measure, in absolute terms, the free sulfite and each of the other sulfite-derived substances in a food, FDA has determined that no such method exists, and that it is unlikely that one will be developed in the near future. Therefore, FDA has selected the Monier-Williams method, which for years has been the standard against which the accuracy of newer procedures has been judged, as the basic method that it will use for enforcement of the sulfite labeling rule.

The agency recognizes that the Monier-Williams method (Ref. 49) was not originally intended to measure sulfite levels as low as 10 ppm. However, FDA has made some procedural changes in the method that, without changing the method's chemical principles, improve its accuracy and reproducibility and thus make it suitable for use at 10 ppm. These changes, as well as other technical aspects of the analytical methodology, are discussed in detail in "A Report on the Monier-Williams Method for Sulfites in Food" (Monier-Williams Report), prepared by FDA (Ref. 50). A copy of this report is on file in the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857. The modified procedure is described in "Monier-Williams Procedure (with Modifications) for Sulfites in Food" (November 1985) and is also on file in the Dockets Management Branch (Ref. 51). The method is also cited as the official regulatory method for sulfite determination (Ref. 8).

B. Citizen Petition

On October 28, 1982, the agency received a citizen petition signed by three consumers, a physician, a scientist, and representatives of the Center for Science in the Public Interest (CSPI), Washington, DC. The petitioners requested that FDA "amend certain food standards and rescind certain food additive regulations, prior sanctions, and advisory opinions that permit the use of sulfiting agents above 350 micrograms per serving." The petitioners also requested that FDA "require warning labels on those products in which sulfiting agents must be used in greater amounts in order to perform essential public health functions."

The petitioners also requested that FDA ban the use of sulfiting agents in drugs designed for the treatment of asthma and either ban their use in over-the-counter and prescription drugs or require a warning label on those drugs in which sulfiting agents were used to perform essential public health functions.

In supplements to the citizen petition that were submitted on March 15, 1983, and August 17, 1983, the petitioners requested that FDA ban the use of sulfiting agents on salad bars, withdraw the prior sanction permitting the use of sodium bisulfite on potatoes, and institute appropriate enforcement action against certain misbranded products labeled for use on vegetable salads or dehydrated fruits and vegetables. The petitioners submitted data to support their claim that vegetable salads and potatoes are significant sources of thiamine, and that products instructing users to apply sulfiting agents to these foods are misbranded. The petitioners suggested that FDA issue an appropriate regulatory letter to all manufacturers of such products.

The petitioners stated that FDA had failed to present any evidence to justify the use of a fifteenfold margin of safety with regard to sulfiting agents. They asked that FDA ensure the existence of a hundredfold safety margin, citing in support of their request the fact that current usage levels posed a significant problem to many consumers, and that interspecies variations in in vivo sulfite oxidase levels have been documented.

The petitioners stated that FDA, in its July 9, 1982, proposal, had not reviewed all of the available scientific data on sulfiting agents. The petitioners submitted references to various published articles, abstracts, and letters concerning adverse reactions to sulfites. In addition, the petition contained information about, and references to, mutagenic in vitro tests and cocarcinogenicity studies of the sulfiting agents.

The petitioners contended that safe alternatives to sulfiting agents, such as ascorbic or citric acid, are available and should be used if necessary. They expressed their belief that proper handling and storage conditions could also, in some instances, obviate the need for sulfiting agents.

On July 25, 1986, the petitioners sent a supplementary comment to Department of Health and Human Services Secretary Bowen emphasizing that 60 percent of the reported sulfite reactions classified by FDA as "serious" involved foods other than fresh fruits and vegetables. The petitioners urged the agency to immediately decide the safety of all remaining uses of sulfites.

FDA has already responded to aspects of the petition in the rulemakings on sulfite labeling (Refs. 7 and 8) and on the use of sulfiting agents on fresh fruits and vegetables (Ref. 9), on potatoes (Ref. 10), and on drugs (51 FR 43900). Thus, for the purposes of this rulemaking, the agency believes that it need not respond to those aspects of the petition. Here, the agency is responding to the remaining parts of this petition and its supplements.

FDA has tentatively decided to deny the petitioners' request that the agency prohibit the use of sulfiting agents on foods at levels of more than 350 micrograms per serving. FDA agrees with the conclusions of the Panel and believes that the uses of sulfiting agents, except for those that have already been addressed because of concern for allergic-type responses in sulfite-sensitive individuals, are GRAS.

FDA reviewed all the scientific references and medical reports cited in the petition and also made them available to the Panel. Furthermore, the agency conducted its own update of the scientific literature on sulfiting agents from 1975 to the present and evaluated the pertinent references on sulfites that it found. The agency also forwarded these data to the Panel for use in its reexamination of sulfites. Thus, both the agency and the Panel have had access to all the relevant data available on sulfites. On the basis of these data, the Panel concluded, and the agency concurs, that certain uses of sulfiting agents on food can no longer be considered to be GRAS, while other uses can still be considered to be GRAS.

The agency has acted to protect sulfite-sensitive individuals in the population from the greatest sources of risk from inadvertent exposure to sulfites, namely, their use on fresh fruits and vegetables and on "fresh" potatoes. However, FDA believes that the totality of data reviewed by the Panel and by the agency confirms the GRAS status, with specific limitations, of most of the remaining uses of sulfites that are not limited by regulation. The agency believes that the petitioners have not provided any data that would justify a tentative conclusion different than the one the agency has reached—that these remaining uses of sulfiting agents are GRAS.

In response to the July 25, 1986, submission from the petitioners, the agency notes that the most recent data on allergic-type responses allegedly caused by sulfiting agents show that over 48 percent of the serious responses are attributable to the use of sulfites on fresh fruits and vegetables. Another 13 percent were allegedly caused by their use on potatoes, which FDA addressed in a recent proposal (52 FR 46968) (Ref. 10). The remaining 39 percent are allegedly attributable to sulfite use in a variety of other foods, most of which are now subject to sulfite labeling regulations (51 FR 25012) (Ref. 8). For these latter uses, the comments of the two groups of experts with whom FDA has consulted (Refs. 2 and 6) indicate that there continues to be a consensus that these uses are GRAS, so long as the sulfites are used in accordance with appropriate limitations, and their presence is properly declared on the label.

The agency believes that any remaining risks to sulfite-sensitive individuals are largely controlled by the sulfite labeling of food. The agency has traditionally relied on ingredient labeling of food as the best means of ensuring that a subpopulation of sensitive individuals will be able to avoid certain food ingredients that are of no safety concern to the general population. (See, for example, Refs. 52 a through c.) If sulfite-sensitive individuals pay attention to labeling, they will be aware when they are in settings in which foods are not ordinarily labeled, such as in restaurants, that certain foods are likely to contain sulfites.

The agency's policy on the labeling of foods that contain sulfites makes clear that when a sulfiting agent is present in a detectable amount in a finished food, regardless of whether the sulfiting agent has been directly added or indirectly added in one or more of the ingredients of the food, it is present in that food at a significant level and must be declared on the label. The July 9, 1986, labeling rule defines a detectable amount of sulfiting agent to be 10 ppm sulfur dioxide equivalents in the finished food product. Because of this rule, persons who know that they are sensitive to sulfites can be more selective in the types of packaged foods that they purchase. By reading the labels on foods, they will be able to avoid the potential hazard of an allergic-type response to sulfites in packaged foods.

Use of the 10 ppm level is a more practicable and enforceable way of determining the sulfite content of food for compliance purposes than is the petitioners' 350 micrograms per serving suggestion. The 10 ppm level does not depend on the weight of a "serving" of a particular food, a quantity that is known to vary greatly from person to person and from food to food. In addition, 10 ppm, as measured in the food, is the lowest level of sulfites in food that can be routinely measured using current analytical methodology (such as the improved Monier-Williams method) (Ref. 8).

The agency stresses that, for consumers who wish to avoid sulfites, existing regulations require that the labeling of most foods that contain these ingredients identify their presence by listing them in the list of ingredients. The agency notes that under existing regulations (21 CFR 101.100(a)(2)) even foods that are presented in unpackaged form in bulk to consumers, such as bulk dried fruit or sulfited bulk shrimp in food stores, must also be appropriately labeled for sulfite content. Such a requirement is consistent with 21 CFR 101.22(e), which requires that bulk foods offered for sale unpackaged must be appropriately labeled. The required information may be displayed to the purchaser on either: (1) the labeling of the bulk container plainly in view; or (2) a counter sign, card, or other appropriate device bearing information that the food being offered for sale contains sulfiting agents. Because it believes that this requirement is a central condition of GRAS status for the use of sulfiting agents, the agency is emphasizing the current requirements regarding labeling of bulk foods by incorporating language similar to that in §§ 101.22(e), 101.100(a)(2), and in paragraph (c)(2) of proposed § 184.1861 as a specific limitation on the use of sulfites. For the same reason, the agency is including language concerning the listing of sulfites on labels for packaged food in paragraph (c)(3) of proposed § 184.1861.

In relation to the petitioners' concerns about safety margins for sulfites, the agency has tentatively concluded that an adequate margin of safety exists between the highest no-observed-adverse-effect level for sulfites from toxicological tests and chronic intake levels of individuals. As discussed above, the Panel has demonstrated, and the agents has confirmed, that a safety margin of at least 100 for estimated chronic intake of sulfites is likely to exist. (This margin of 100 is the same as the traditional hundredfold safety factor chosen for the safe use of any new food additive based entirely on long-term animal test results with no previous experience of use in the food supply.)

The agency believes that it is not appropriate to calculate a safety margin for a food ingredient by comparing no-observed-adverse-effect levels from chronic animal feeding studies with highly exaggerated, acute levels of intake of the ingredient that may occur when a consumer ingests an occasional hypothetical meal containing large amounts of the ingredient. Such exaggerated exposures are not likely to be part of a chronic dietary pattern and are likely to be of concern only to certain sulfite-sensitive individuals. To protect such individual, FDA has, as noted above, undertaken separate rulemakings. These actions have served to reduce the unexpected exposures to sulfites via the foods that have caused

the greatest concern for the public health.

Thus, the agency believes that the current safety margin, based on chronic exposure to sulfites in foods that are the subject of the present rulemaking, is adequate and is consistent with the continued GRAS status of those uses of sulfiting agents that the petitioner had requested that FDA ban.

VII. Conclusions

A. Specific Limitations on Residual Sulfite Levels

The agency has reviewed all of the available relevant data and information concerning the uses of sulfiting agents in food. It tentatively concludes that certain uses of sulfiting agents in food are GRAS with specific limitations.

The Panel's first conclusion about the safety of sulfiting agents, with which the agency concurs, states that "* * * it is not possible to determine, without additional data, whether a significant increase in consumption would constitute a dietary hazard." This portion of the Panel's conclusions is analogous to the second of the five usual evaluation statements that the Select Committee has traditionally used in evaluating substances in the GRAS review (Refs. 2 and 3).

The agency's usual action in response to this type of conclusion is to affirm the substance as GRAS but to impose specific limitations on the conditions under which the substance may be added to foods. Thus, in the accompanying regulations, the agency is specifying the food categories on which sulfites may be used, the maximum levels of residual sulfites on finished food products in each category, and the condition that the use of sulfites be declared on the label of the finished food.

1. Food Categories and Maximum Levels as Specific Limitations

In general, the food categories included in the table of limitations in proposed § 184.1861(c) derive from the agency's examination of reported uses of sulfites compiled from the following sources: the 1982 proposal and comments on it received by FDA; the 1977 NAS survey on the use of food additives; and the Panel's report (Refs. 1, 5, and 6, respectively). To determine the appropriate limitations, the agency examined available data on sulfite residue levels in each relevant finished food product. The agency then specified a level for each limitation that represents the maximum level of sulfites for each use consistent with: (1) current good manufacturing practice (CGMP) and (2) the range of levels that have been reported for given food products.

Establishing a specific limitation, of course, does not mean that food processors necessarily ought to use the maximum allowed amounts in their particular applications. Although most of the specific limitations set forth in proposed § 184.1861(c) encompass the range of reported use levels of sulfites under CGMP for each food category, food processors should use no more sulfite than is necessary to accomplish the intended technical effect. The agency solicits comments from all interested parties on the appropriateness of any of the specific limitations on sulfite residue levels set forth in the proposed regulation.

The following examples are representative of the agency's reasoning for establishing certain sulfur dioxide equivalent levels for the various food categories in proposed § 184.1861(c).

To establish limitations for sulfites in wine, the agency has relied primarily on BATF Notice Number 543 (49 FR 37527) (Ref. 53). In that notice, BATF proposed that all wines having a total sugar content of 5 or more grams per 100 milliliters may contain up to 275 ppm of sulfites expressed as sulfur dioxide equivalents.

For tea, the agency is aware from previously submitted data that some exceedingly high levels of sulfites (residue levels of over 1,000 ppm) have been reported in certain tea and tea products. Most comments regarding the use of sulfites in tea, however, reported considerably lower levels, not exceeding 90 ppm. The agency believes, based on the evidence available to it, that a limitation of 90 ppm on tea is appropriate.

For fried fruit, the agency is aware that levels of sulfite use vary greatly. The agency is aware of reports of levels of sulfites added to apricots ranging from 2,000 to 3,500 ppm and residual levels of sulfites in apricots ranging from 1,000 to 1,750 ppm (Ref. 6, p. 14). The agency believes, on the basis of information received from the industry, that an overall level of 2,000 ppm for dried fruits is adequate, even for uses such as in dried apricots, because this level reflects what the agency believes has traditionally been the highest use level of sulfites in dried fruit (Refs. 5 and 6). In fact, the United Nations Food and Agriculture Organization and the World Health Organization Joint FAO/WHO Food Standards Programme, under the Codex Alimentarius Commission, prescribed a level of 2,000 ppm for dried apricots (Ref. 54). Other uses of sulfiting agents in the production of dried fruit, for example in the production of raisins, require sulfite residues of less than 2,000 ppm (Refs. 5 and 6).

The agency is including dehydrated, canned, and frozen potatoes in § 184.1861(c) even though in the rulemaking on sulfites and potatoes, the agency is inquiring about the safety of these uses. These actions are not inconsistent because in § 184.1861(c), the agency is proposing to establish specific limitations that restrict the GRAS affirmation of these uses to those situations in which the sulfites are used at the appropriate levels, and in which the presence of the sulfites is declared on the label of the food. In the other rulemaking (52 FR 46968), FDA is inquiring about the use of sulfites in or on canned, dehydrated, or frozen potatoes when the food is intended to be served or sold unpackaged and unlabeled to consumers.

2. Labeling as a Specific Limitation

Under section 409(c)(1) of the act (21 U.S.C. 348(c)(1)), FDA is authorized, in approving the use of a food additive, to list the conditions under which the additive may be safely used. These conditions may include any labeling requirements that the agency deems necessary to assure the safe use of the additive.

Similarly, under 21 CFR 184.1(b)(2), in affirming a substance as GRAS, FDA is authorized to set forth, by means of specific limitations, the particular conditions, including labeling, under which there is general recognition among qualified experts that use of the substance is safe. After careful review of the evidence on the use of sulfiting agents, FDA has tentatively concluded that the use of these ingredients is GRAS only (except in the restaurant-type setting) when the conditions of their use includes a declaration on the label or labeling of the presence of the sulfiting agents in the food.

The agency believes that package labeling, the banning of the use of sulfiting agents on fresh fruits and vegetables, and the action that FDA is proposing with regard to "fresh" potatoes (52 FR 46968) will remedy the conditions that have produced most of the allergic-type reactions to sulfites in restaurant settings. Thus, the agency believes that there is no basis to find that unlabeled use of products containing sulfites in restaurant settings is not GRAS. However, FDA invites comments on this issue.

The basis for FDA's tentative conclusion is provided by the data that have been discussed in this document. FDA has received numerous reports of sulfite-sensitive individuals who have

suffered allergic-type reactions because they ate foods that they did not realize were sulfited. The best way to prevent reactions of this type is to advise the consumer of the presence of the sulfites. If such information is provided in the label or labeling, sulfite-sensitive individuals will be able to avoid foods that contain these ingredients.

In recognition of the importance of such information, FDA is proposing to establish as a specific limitation in § 184.1861(c) that for the use of sulfiting agents in foods in bulk containers or in packaged foods to be GRAS, the presence of these ingredients must be declared on the label or labeling of those foods. As noted earlier, the requirement concerning the ingredient labeling of bulk foods is not a new requirement. The inclusion of this requirement in § 184.1861(c) simply emphasizes an existing requirement (see 21 CFR 101.22(e) and 101.100(a)(2)).

If the agency adopts the specific limitations that it has proposed, sulfites must be used in accordance with these limitations, or their addition to food will be considered by FDA to constitute the use of an unapproved food additive (see 21 CFR 184.1(b)(2)).

B. Claims of Prior Sanctions

The agency has received several submissions claiming that sulfites were used in specific foods in accordance with a sanction or approval granted before September 6, 1958, and that those uses are "prior sanctioned." The submissions include the GMA report, the citizen petition for the recognition of a prior sanction for the use of sulfites in maraschino cherries and glacé fruits from the Maraschino Cherry and Glacé Fruit Processors Association, and the citizen petition for the recognition of a prior sanction for the use of sulfites in beer and other malt beverages from the Beer Institute.

The agency has reviewed these submissions and has the following responses:

1. Claims for Glacé Fruit and Maraschino Cherries

The petition for maraschino cherries and glacé fruit (FAP 6CP3941) presented arguments that these products are covered by both an explicit and a general prior sanction. The petition stated that sulfur dioxide has been used to produce maraschino cherries since 1923. In addition, the petition cited numerous actions that it claimed evidenced that this use had been sanctioned by the government. In 1934, USDA promulgated a grade standard for "sulfured cherries", which were defined as cherries prepared in a solution of sulfur dioxide. In 1938, an FDA letter acknowledged that sulfites could be used to prepare brine cherries. No specific limits were listed. In 1942, FDA issued a standard of identity for fruit cocktail that permitted the inclusion of maraschino cherries. In 1943, FDA expressly approved the use of sulfur dioxide and sulfurous acid in preserving citrus foods. In a number of other letters before 1958, FDA officials acknowledged that sulfites could be used in processing cherries and other fruits. No specific limitations were listed for any of these processes.

Because no specific limits were listed in any of the correspondence submitted in the petition, the agency concludes that this use of sulfiting agents was consistent with current good manufacturing practices. A 1941 document submitted with the petition stated that residual levels of sulfites in the finished product was usually in the range of 15 to 20 ppm, and that an absolute maximum would be 50 ppm in the finished cherry (FAP 6CP3941, p. 124). Additionally, a 1983 letter submitted with the petition described a survey in which analysis of 39 samples of maraschino cherries showed that 29 samples contained less than 10 ppm sulfur dioxide. Nine samples contained sulfur dioxide levels ranging from 61 to 141 ppm, and one sample contained 203 ppm sulfur dioxide (FAP 6CP3941, p. 93). Also, this letter stated that the State of Pennsylvania has a regulation prohibiting more than 150 ppm sulfur dioxide in maraschino cherries (FAP 6CP3941, p. 92).

FDA has reviewed this petition and tentatively accepts that the use of sulfiting agents on maraschino cherries and glacé fruit is covered by a prior sanction. However, consistent with its tentative determination that this use is GRAS, the agency will include this use in § 184.1861 with specific limitations.

The petitioners for maraschino cherries provided evidence that the typical residual level of sulfites in maraschino cherries is approximately 50 ppm in the finished product. This level is lower than the level of 150 ppm reported to NAS in the 1977 Survey of Industry on the Use of Food Additives (Ref. 5). The level reported to NAS reflects a plausible upper limit to a range of possible uses, depending upon the needs of the food processor. The agency is proposing that this level of 150 ppm sulfur dioxide equivalents in finished maraschino cherries be the maximum residual level allowed in that food because that level encompasses a range of food-processing practices that are consistent with current good manufacturing practice for sulfiting maraschino cherries and glacé fruits. Because the level of 150 ppm sulfur dioxide equivalent exceeds the typical level claimed as a prior-sanctioned use in the citizen petition, the agency believes that it would serve no useful purpose to amend 21 CFR Part 181 to document a prior-sanctioned use at a lower level. The agency therefore tentatively rejects the petitioner's request to amend 21 CFR Part 181 to include a prior sanction for the use of sulfites in maraschino cherries or glacé fruits.

2. Claims for Beer

The petition from the Beer Institute (FAP 6CP3960) contained copies of several letters and memoranda from FDA dated before 1958 that gave explicit approval for the use of sulfiting agents in beer. In several of these documents a residual maximum limit of 25 ppm was stated.

The agency has reviewed this submission and tentatively concludes that the use of sulfites in beer is covered by a prior sanction. The agency also finds that there is an appropriate basis to conclude that this use is GRAS. Moreover, the reviews by two expert groups (Refs. 2 and 6) indicate that a consensus continues to exist that the use of sulfites in beer is GRAS. Therefore, FDA has tentatively decided not to amend 21 CFR Part 181 to reflect a prior sanction for the use of sulfites in beer. Instead, FDA is listing this use in the proposed GRAS affirmation regulation.

Based on information obtained from the brewing industry and from BATF, FDA believes that a specific limitation of 25 ppm sulfur dioxide equivalents in beer adequately represents current good manufacturing practice for virtually all commercially brewed beers. It is true that some recent data from a BATF survey of beers indicate that most beers contain no more than 15 ppm sulfur dioxide equivalents (Ref. 55). However, in view of the apparent prior sanction for the use of sulfites in beer at 25 ppm sulfur dioxide equivalents, the agency has tentatively concluded that it would not be appropriate to adopt the 15 ppm level. The agency welcomes comments and data from interested parties concerning appropriate levels of sulfur dioxide equivalents in beer.

3. The GMA Report

The agency has also reviewed the report from GMA that provides documentation of specific claimed prior sanctions for the use of sulfites in food.

GMA's argument in support of a general prior sanction for the use of

sulfites in foods is based essentially on the following:

(1) In 1908, FDA issued Food Inspection Decision (FID) 89, which authorized the use of sulfites in foods in ordinary quantities to achieve their functional effect.

(2) In 1940, in a letter to industry, FDA stated that it was still being guided by FID 89 with respect to food uses of sulfites.

(3) In correspondence before 1958, FDA sanctioned the use of sulfites in foods. In some of these letters, FDA expressed limitations on the use of sulfites in food. These limitations were generally that: (i) Sulfites could not be used in foods that were good sources of vitamin B_1; (ii) sulfites could not be used in standardized foods where the standard did not provide for the use of sulfites; and (iii) sulfites could not be used in meat, because they concealed damage or inferiority.

(4) In correspondence before 1958, FDA also explicitly sanctioned specific uses of sulfites in specific categories of food, including dehydrated potato products; precut peeled potatoes; bakery products; beer and malt beverage; "beverages" in general; cherries; citrus foods; coconut; corn products; dehydrated fruits and vegetables; fresh fruits and vegetables; gelatin; molasses; mushrooms; onion and garlic products; pickles and pickled vegetables; sauerkraut and horseradish; shrimp; soft drinks; syrups; and wine and wine vinegar, and as a dough conditioner.

The agency recognizes that the use of sulfites in many foods predates 1958, and that the use of one or more of the sulfiting agents in many food categories may be the subject of a prior sanction. The agency has become aware, however, that certain uses of sulfites in some foods (for example, in fresh fruits and vegetables) may render the food injurious to health and cause the food to be adulterated under section 402(a)(1) of the act (Refs. 9a and 9b). Because some uses have been found to be unsafe under section 402(a)(1) of the act, a general prior sanction, as might be implied from some FDA correspondence before 1958, is not consistent with the safe use of these ingredients (see 21 CFR 181.5(c)). Therefore, FDA is proposing herein to revoke any such general prior sanction.

Having tentatively concluded that any general prior sanction that may have existed should revoked, the agency turns to specific prior sanction claims made by GMA. The agency will address each claim on a case-by-case basis. Moreover, FDA requests that any other claims of prior sanctions for specific uses of sulfites in food be brought to its attention as comments on this proposal. The agency will consider these claimed prior sanctions based on the available evidence.

The agency compared the uses and limitations that it has tentatively concluded can be affirmed as GRAS to the uses and levels that GMA has claimed are prior-sanctioned. FDA is proposing to affirm as GRAS, at use levels equal to or greater than those in the GMA report, many of the uses of sulfites that are the subject of GMA's claims. These uses include the use of sulfites on bakery products, beer and malt beveages, certain cherries, citrus foods, coconut, corn products, most dehydrated fruits and vegetables, gelatin, molasses, onion and garlic products, shrimp, syrups, and wine vinegar and the use of sulfites as a dough conditioner. For these uses, the agency believes that there is no need to determine whether there is a prior sanction and no reason to promulgate separate, redundant regulations under 21 CFR Part 181.

GMA also presented evidence for the use before 1958 of sulfites in "beverages" and "soft drinks." In 1940, FDA issued a letter that stated that sulfur dioxide could be used in beverages at a level of up to a "few hundred parts per million." Additionally, in other publications and letters dated before 1958, FDA stated that sulfites may be used with no specific limits in carbonated beverages and beverages. In 1963, FDA proposed a standard of identity for soda water that permitted the use of sulfites as optional ingredients. This standard was codified in 1966 (21 CFR 31.1(b)(10)). This standard was revised in 1975 (40 FR 26267; June 23, 1975). Since that revision, the soda water standard (now 21 CFR 165.175) does not specifically list sulfites but provides for the optional use of any safe and suitable ingredient.

The agency has reviewed this evidence and acknowledges that a prior sanction exists for the use of sulfites in soft drinks. However, FDA has no information that U.S. soft drink manufacturers intentionally add sulfites to such beverages. Therefore, the agency is taking no action on this prior sanction at the present time. Instead, the agency solicits comments from interested parties concerning this use of sulfiting agents. The agency is particularly interested in the amounts of sulfites used. Based on the information that is submitted, the agency will decide if this use should be GRAS or codified in 21 CFR Part 181.

The GMA report lists as prior sanctioned the use of sulfites in maraschino cherries at 300 ppm. GMA has not presented evidence of explicit approval of such use by the agency (see 21 CFR 181.5(a)). Rather, it has inferred a sanction based on an industry-prepared memorandum of a meeting with an FDA official. The agency tentatively concludes that this evidence does not provide an adequate basis on which to establish a prior sanction.

The citizen petition from the Maraschino Cherry and Glace Fruit Processors Association provides more extensive and direct documentation of FDA's historical approach to industry practices regarding the production of maraschino cherries. That petition, as stated above, claims that the usual residual sulfite level in maraschino cherries is approximately 50 ppm in the finished product. The limitation for maraschino cherries that FDA is proposing in § 184.1861 is 150 ppm and encompasses the likely range of sulfite levels under current good manufacturing practice for such cherries.

Neither the Panel report nor the 1977 NAS survey reveals any use of sulfites in dairy products. Additionally, there appear to be no data to indicate that sulfites are currently being used on any dairy products. However, in its report, GMA claims that before 1958, the agency permitted use of sulfites in cheese and other dairy products. GMA cites a 1947 letter from FDA to a major producer of cheese products regarding the use of sulfur dioxide in food, an FDA file note in 1957 that stated "sodium metabisulfite entirely safe, cheese," and a letter to the Ohio State Department of Agriculture in which FDA stated that "sodium bisulfite is not considered to be directly harmful in such amounts as are generally used in foods."

The agency has reviewed this evidence. Nowhere in the two letters did the agency state that the use of sulfites is safe for use in dairy products. The agency is of the opinion that these letters were nothing more than responses to general letters of inquiry relating to sulfites. As such, these letters do not constitute a prior sanction.

With regards to the statement in the FDA file note, the agency does not believe that this file note can be construed as the type of "sanction or approval" that would provide the basis for the finding of a prior sanction because it does not represent an explicit statement of agency approval. Therefore, FDA tentatively concludes that there is no basis for finding a prior sanction for the use of sulfites in dairy products.

In support for its claim of a prior sanction for the use of sulfites in pickles and pickled vegetables, GMA cited a 1938 letter from FDA to industry that

stated in part: "* * * relative to the use of sulphur dioxide as a preservative for pickles and similar products, our law enforcement activities have not included technological investigations along such lines." A 1953 letter from FDA to industry sanctioned the use of sulfites in pickled vegetables at no more "than 300 parts per million in the finished article" (Ref. 56). The vegetables to be pickled were not specified.

In a 1945 letter from FDA to industry, the use of sulfur dioxide in horseradish and sauerkraut was addressed. Also, in a 1953 letter from FDA, the agency stated: "We are not in a position to object to the use of sulphur dioxide in small quantities in sauerkraut, provided its presence is declared on the labeling as a preservative." In both of these letters the agency cautioned that FDA discourages the use of preservatives in the manufacture of any food product when current good manufacturing practices would eliminate the need for the use of such ingredients.

The agency acknowledges that a prior sanction exists for the use of sulfites in pickled vegetables on the basis of the 1953 letters and the 1945 letter cited above. However, the agency finds that the 1938 letter cited above does not constitute an appropriate basis for a prior sanction for the use of sulfites in pickled vegetables because the agency was not sanctioning this use in this letter, and because this letter was issued before the effective date of the act.

However, rather than promulgate a prior-sanctioned regulation for the use of sulfites in pickled vegetables, the agency is proposing to codify this use as GRAS in 21 CFR Part 184 in accordance with 21 CFR 184.1(b)(2). Also, the agency is proposing to affirm this use as GRAS at a level lower than the 300 ppm sanctioned in a 1953 letter from FDA because the agency finds that the 300 ppm level of sulfites no longer reflects current good manufacturing practice.

The Panel, using data from the 1977 NAS survey of industry on the use of food additives, reported levels of sulfite addition of 30 ppm to pickles and relishes. The 1977 NAS survey data are the only recent data available on the use of sulfites on such foods. When the agency sanctioned a level of no more than 300 ppm sulfites in the finished article, it was approving a level that reflected then-current good manufacturing practice. However, as manufacturing conditions have improved, the CGMP level for sulfites has decreased steadily. Because present day industry practices result in much lower residual levels of sulfites (30 ppm) than the claimed prior-sanctioned level of 300 ppm, the agency believes that in spite of the evidence supplied by GMA for a prior sanction, the level consistent with GRAS status for this use of sulfites should be set at 30 ppm. Although the agency is proposing to establish a specific limitation of 30 ppm for the use of sulfites on pickles and relishes (including horseradish and pickled vegetables such as sauerkraut), it will consider new data from industry on current good manufacturing practices and other data and information to determine on a case-by-case basis appropriate levels applicable to such uses of sulfiting agents if such data are submitted.

The GMA report cites levels of up to 350 ppm of sulfites in wine as a prior-sanctioned use. The agency tentatively concludes that the evidence supplied in the GMA report does not demonstrate that a prior sanction exists for this use. Three exhibits supplied by GMA contain references to the Alcohol Tax Unit regulations (27 CFR 4.22(b)(1)) of the Bureau of Alcohol, Tobacco and Firearms of the U.S. Department of the Treasury. These references are insufficient to serve as a basis for a prior sanction because section 201(s)(4) of the act says that the use for which a prior sanction is claimed must be "in accordance with a sanction or approval * * * pursuant to this Act, the Poultry Products Inspection Act * * * or the Meat Inspection Act * * *." Treasury Department statutes are not included. The only reference to 350 ppm of sulfites in wine by FDA is contained in an agency document dated September 12, 1938, before the current act became effective on June 25, 1939. Thus, the agency document does not constitute a sanction under section 201(s)(4). Therefore, the agency is tentatively denying GMA's assertion that a valid prior sanction exists for the use of sulfites in wine at 350 ppm.

In the present rulemaking, as explained above, the agency is proposing to set a specific limitation of 275 ppm on sulfites in wine. This level is the same as that proposed by BATF in Notice 543 (49 FR 37527) (Ref. 53). BATF is currently receiving comments on its proposal and is compiling data on the actual levels of sulfites in many brands of commercially available wines. Most of the levels reported thus far are at or below the level of 275 ppm. Thus, the agency tentatively concludes that 275 ppm for sulfites in wine is the appropriate level. The agency will, however, consider industry data on current good manufacturing practices and other data and information to determine levels applicable to such use of sulfiting agents.

VIII. Requests for Comments

Interested persons may, on or before February 17, 1989, submit to the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857, written comments regarding this proposal. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday. In addition to requesting comments concerning the proposal in its entirety, the agency also solicits comments on the economic impact of the proposed action.

IX. References

The following references have been placed on display in the Dockets Management Branch and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. "Sulfiting Agents; Proposed Affirmation of GRAS Status with Specific Limitations; Removal from GRAS Status as Direct Human Food Ingredient," 47 FR 29956, July 9, 1982.

2. Select Committee on GRAS Substances, "Evaluation of Health Aspects of Sulfiting Agents as Food Ingredients," Life Sciences Research Office, Federation of American Societies for Experimental Biology, prepared under FDA contract 223–75–2004, 1976.

3. Select Committee on GRAS Substances, "Insights on Food Safety Evaluation," Life Sciences Research Office, Federation of American Societies for Experimental Biology, prepared under FDA contract 223–81–2394, December 1982, and references cited therein.

4. The Franklin Institute Research Laboratories, Philadelphia, PA, "Monograph on Sulfiting Agents," submitted under Department of Health, Education, and Welfare contract number FDA 72–101, 1972.

5. National Academy of Sciences/National Research Council, "The 1977 Survey of Industry on the Use of Food Additives," prepared under FDA contract 223–77–2025, 1979.

6. Select Committee on GRAS Substances, "The Reexamination of the GRAS Status of Sulfiting Agents," Life Sciences Research Office, Federation of American Societies for Experimental Biology, prepared under FDA contract 223–83–2020, January 28, 1985.

7. "Food Labeling; Proposed Rule Concerning Sulfiting Agents," 50 FR 13306, April 3, 1985.

8. "Food Labeling; Declaration of Sulfiting Agents," 51 FR 25012, July 9, 1986.

9a. "Sulfiting Agents; Proposal to Revoke GRAS Status for Use on Fruits and Vegetables Intended to be Served or Sold Raw to Consumers," 50 FR 32830, August 14, 1985.

9b. "Sulfiting Agents; Revocation of GRAS Status for Use on Fruits and Vegetables

Intended to be Served or Sold Raw to Consumers," 51 FR 25021, July 9, 1986.

10. "Sulfiting Agents; Proposal to Revoke GRAS Status for Use on Potatoes Served or Sold Unpackaged and Unlabeled to Consumers," 52 FR 46968, December 10, 1987.

11. Taylor, S.L., and R.K. Bush, "Sulfites, A Technical and Scientific Review," prepared for International Food Additives Council, Atlanta, 75 pp., 1983.

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X. Economic Impact

FDA has examined the potential economic consequences of this GRAS affirmation regulation in accordance with the Regulatory Flexibility Act and has determined that this regulation will permit most current known uses of sulfiting agents at current use levels. (These uses do not include the use of sulfiting agents on fresh fruits and vegetables intended to be served raw or sold raw to consumers and on "fresh" potatoes served or sold unpackaged and unlabeled to consumers. FDA has considered the economic impact of not

affirming these as GRAS in those rulemakings.)

There may arise a cost to some firms whose products do not meet the specific limitations for sulfites. FDA has received information that some products, especially certain dried fruits, may in some cases be produced with residual sulfite levels in excess of the levels proposed in this document. Although FDA does not have an estimate of the cost that may be associated with reducing these residual sulfite levels, it is aware that dried fruits and other affected products produced according to current good manufacturing practices consistently show residual sulfite levels, well within the ranges proposed in this document. In the absence of any data indicating otherwise, the agency concludes that all manufacturers are capable of producing these products with residual sulfite levels within the levels specified in this proposal, and that any additional costs will be minimal.

In addition, there are a few uses that the agency cannot affirm as GRAS because the agency was unaware of these uses until recently, and, consequently, they were not reviewed or evaluated by either the FASEB Select Committee or the FASEB Ad Hoc Review Panel. These uses include the use of sulfiting agents in home dehydrators and winemaking kits, certain beverages, soft drinks, and dairy products. Although the agency cannot affirm the GRAS status of the use of sulfites in these products based on available information, it is requesting further information regarding these uses. The economic consequences of the agency's decisions regarding the GRAS status of these uses will be evaluated in the final rule.

This proposed regulation will also make clear that as a condition for the GRAS status of the use of sulfites in foods that are presented in unpackaged form in bulk to consumers, the presence of sulfites in those foods must be declared in the labeling or by other appropriate device as required by existing regulations (21 CFR 101.22(e) and 101.100(a)(2)). The most recent U.S. Department of Agriculture estimate indicates that there are approximately 240,000 food stores in the United States. Only a portion of these retail food outlets sell sulfited, unpackaged, bulk food to consumers and would, therefore, be affected by this labeling requirement.

In addition, the labeling may be in the form of a counter sign or card which should pose minimal incremental cost to affected retail food outlets.

In accordance with section 605(b) of the Regulatory Flexibility Act, the agency has considered the effect that this proposed rule, if promulgated, will have on small businesses and has concluded that the regulation will result in a minimal impact on any one firm. Therefore, the agency certifies that no significant impact on a substantial number of entities will be caused by this action.

Furthermore, in accordance with Executive Order 12291, the agency has analyzed the potential economic effects of this regulation and has determined that the rule, if promulgated, is not a major rule as defined by that Order.

The agency, however, solicits comments on the economic impact of the proposed action.

XI. Environmental Impact

The agency has determined under 21 CFR 25.24(b)(7) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an invironmental assessment nor an environmental impact statement is required.

List of Subjects

21 CFR Part 182

Food ingredients, Food packaging, Spices and flavorings.

21 CFR Part 184

Food ingredients.

Therefore, under the Federal Food, Drug, and Cosmetic Act, it is proposed that Parts 182 and 184 be amended as follows:

PART 182—SUBSTANCES GENERALLY RECOGNIZED AS SAFE

1. The authority citation for 21 CFR Part 182 continues to read as follows:

Authority: Secs. 201(s), 402, 409, 701, 52 Stat. 1046–1047 as amended, 1055–1056 as amended, 72 Stat. 1784–1788 as amended (21 U.S.C. 321(s), 342, 348, 371); 21 CFR 5.10, 5.61.

§§ 182.3616, 182.3637, 182.3739, 182.3766, 182.3798 and 182.3862 [Removed]

2. Part 182 is amended by removing § 182.3616 *Potassium bisulfite,* § 182.3637 *Potassium metabisulfite,* § 182.3739 *Sodium bisulfite,* § 182.3766 *Sodium metabisulfite,* § 182.3798 *Sodium sulfite,* and § 182.3862 *Sulfur dioxide* from Subpart D.

PART 184—DIRECT FOOD SUBSTANCES AFFIRMED AS GENERALLY RECOGNIZED AS SAFE

3. The authority citation for 21 CFR Part 184 continues to read as follows:

Authority: Secs. 201(s), 402, 409, 701, 52 Stat. 1046–1047 as amended, 1055–1056 as amended, 72 Stat. 1784–1788 as amended (21 U.S.C. 321(s), 342, 348, 371); 21 CFR 5.10, 5.61.

4. New § 184.1861 is added to Subpart B to read as follows:

§ 184.1861 Sulfiting agents.

(a) Sulfiting agents are sulfur dioxide (SO_2, CAS Reg. No. 7446–09–5), sodium sulfite (Na_2SO_3, CAS Reg. No. 7757–83–7), sodium metabisulfite ($Na_2S_2O_5$, CAS Reg. No. 7681–03–7), anhydrous sodium bisulfite (which is a mixture of sodium bisulfite ($NaHSO_3$ (CAS Reg. No. 7631–90–5)) and $Na_2S_2O_5$,), potassium metabisulfite ($K_2S_2O_5$, CAS Reg. No. 16731–55–8), and anhydrous potassium bisulfite (which is a mixture of potassium bisulfite ($KHSO_3$ (CAS Reg. No. 7773–03–7)) and $K_2S_2O_5$,).

(b) Sulfur dioxide, sodium sulfite, sodium metabisulfite, anhydrous sodium bisulfite, and anhydrous potassium metabisulfite meet the specifications of the Food Chemicals Codex, 3d Ed. (1981), pp. 316, 303, 289, 279, and 247, respectively, which is incorporated by reference in accordance with 5 U.S.C. 552(a). Copies may be obtained from the National Academy Press, 2101 Constitution Ave. NW., Washington, DC 20418, or are available for inspection at the Office of the Federal Register, 1100 L St. NW., Washington, DC. FDA is developing food-grade specifications for anhydrous potassium bisulfite in cooperation with the Food Chemicals Codex Committee of the National Academy of Sciences. In the interim, the ingredient must be of a purity suitable for its intended use.

(c) In accordance with § 184.1(b)(2), the ingredients are used as antimicrobial agents, antioxidants, and bleaching agents to treat food only within the following specific limitations:

(1) The ingredients may be used only in the following food categories at the following maximum residual sulfur dioxide equivalent levels:

Category of food	Maximum residual sulfur dioxide equivalent level [1]
Baked goods, § 170.3(n)(1) of this chapter.	30 ppm.
Beer, § 170.3(n)(2) of this chapter.	25 ppm.
Wine, § 170.3(n)(2) of this chapter.	275 ppm.
Tea, § 170.3(n)(7) of this chapter.	90 ppm.
Condiments and relishes, § 170.3(n)(8) of this chapter.	30 ppm.
Vinegar, § 170.3(n)(8) and (26) of this chapter.	75 ppm.
Dairy product analogs, § 170.3(n)(10) of this chapter.	200 ppm.
Processed seafood products, other than dried or frozen, § 170.3(n)(13) of this chapter.	25 ppm.

Category of food	Maximum residual sulfur dioxide equivalent level [1]
Dried fish, § 170.3(n)(13) of this chapter.	200 ppm.
Shrimp, fresh and frozen, § 170.3(n)(15) of this chapter.	100 ppm.
Lobster, frozen, § 170.3(n)(15) of this chapter.	100 ppm.
Gelatin, § 170.3(n)(22) of this chapter.	40 ppm.
Grain products, § 170.3(n)(23) of this chapter.	200 ppm.
Gravies and sauces, § 170.3(n)(24) of this chapter.	75 ppm.
Jams and jellies, § 170.3(n)(28) of this chapter.	30 ppm.
Nut products, § 170.3(n)(32) of this chapter.	25 ppm.
Plant protein isolates, § 170.3(n)(33) of this chapter.	110 ppm.
Dried fruit, § 170.3(n)(35) of this chapter.	2,000 ppm.
Fruit juices, § 170.3(n)(35) of this chapter.	1,000 ppm in concentrates. 300 ppm in regular strength juices.
Glacé fruit, § 170.3(n)(35) of this chapter.	150 ppm.
Maraschino cherries, § 170.3(n)(35) of this chapter.	150 ppm.
Dehydrated vegetables § 170.3(n)(36) of this chapter.	200 ppm.
Dehydrated potatoes, § 170.3(n)(36) of this chapter.	500 ppm.
Vegetables, canned, § 170.3(n)(36) of this chapter.	30 ppm.
Frozen potatoes, § 170.3(n)(36) of this chapter.	50 ppm.
Vegetable juice, § 170.3(n)(36) of this chapter.	100 ppm.
Filled crackers, § 170.3(n)(37) of this chapter.	75 ppm.
Soup mixes, § 170.3(n)(40) of this chapter.	20 ppm in dry mix.
Sugar, § 170.3(n)(41) of this chapter.	20 ppm.
Sweet sauces and syrups, § 170.3(n)(43) of this chapter.	60 ppm.
Molasses, § 170.3(n)(43) of this chapter.	300 ppm.

[1] Residues in the finished food products are to be determined by sections 20.123 through 20.125, "Total Sulfurous Acid," in the "Association of Official Analytical Chemists," 14th Ed. (1984), which is incorporated by reference in accordance with 5 U.S.C. 552(a), and the refinements of the "Total Sulfurous Acid" procedure in "Monier-Williams Procedure (with Modifications) for Sulfites in Food," November 1985. This procedure is Appendix A to Part 101 of this chapter.

(2) For sulfited foods that are received in bulk containers and not in package form, including all foods for which a definition and standard of identity have been prescribed by regulation, the use of sulfite in such foods shall be declared to the purchaser either (i) in the labeling of the bulk container plainly in view or (ii) in a counter sign, card, or other appropriate device bearing the information that the product has been treated with sulfites.

(3) For sulfited foods in packaged form, including all foods for which a definition and standard of identity have been prescribed by regulation, the use of sulfite in such food shall be declared on the label.

(d) The ingredients are not generally recognized as safe for use: (1) in meats; (2) in food recognized as a source of vitamin B_1; and (3) on fruits or vegetables intended to be served raw to consumers or sold raw to consumers, or to be presented to the consumer as fresh.

Frank E. Young,

Commissioner of Food and Drugs.

Otis R. Bowen,

Secretary of Health and Human Services.

Dated: August 22, 1988.

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